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<b>(21) International Application Number:</b> PCT/US94/10140 <b>(22) International Filing Date:</b> 7 September 1994 (07.09.94) <b>(30) Priority Data:</b> 08/162,809      3 December 1993 (03.12.93)      US  <b>(71) Applicant:</b> LA JOLLA CANCER RESEARCH FOUNDATION [US/US]; 10901 North Torrey Pines Road, La Jolla, CA 92037 (US).  <b>(72) Inventors:</b> PASQUALE, Elena, B.; 6105 Dirac Street, San Diego, CA 92122 (US). SAJJADI, Fereydoun, G.; 1548 Plumtree Drive, Encinitas, CA 92024 (US).  <b>(74) Agents:</b> IMBRA, Richard, J. et al.; Campbell and Flores, Suite 700, 4370 La Jolla Village Drive, San Diego, CA 92122 (US).		<b>(81) Designated States:</b> CA, JP, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).  <b>Published</b> <i>With international search report.</i>
<b>(54) Title:</b> NOVEL Eph-RELATED TYROSINE KINASES, NUCLEOTIDE SEQUENCES AND METHODS OF USE  <b>(57) Abstract</b>  The invention provides substantially purified Eph-related protein tyrosine kinases, or functional fragments thereof, having about 23 to 66 percent amino acid sequence identity in their carboxyl terminal variable regions compared to known members of the Eph subclass of tyrosine kinases. Nucleic acids encoding such Eph-related protein tyrosine kinases, vectors and host cells are also provided. The invention also provides a method of diagnosing cancer and determining cancer prognosis. For example, the method provides for removing a tissue or cell sample from a subject suspected of having cancer and determining the level of Eph-related protein tyrosine kinase in the sample, wherein a change in the level or activity of an Eph-related protein tyrosine kinase compared to a normal sample indicates the presence of a cancer or indicates the level of malignancy of a cancer.		

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**NOVEL Eph-RELATED TYROSINE KINASES, NUCLEOTIDE  
SEQUENCES AND METHODS OF USE**

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HD 26351 and CA 56721. Accordingly, the United States  
5 government has certain rights in the invention.

**BACKGROUND OF THE INVENTION**

This invention relates generally to protein  
tyrosine kinases and, more particularly, to Eph-related  
receptor tyrosine kinases and their manipulation for the  
10 control of cellular processes.

Receptor tyrosine kinases comprise a large family  
of proteins that share a number of structural features such  
as a glycosylated extracellular ligand-binding domain, a  
hydrophobic transmembrane domain and a conserved  
15 cytoplasmic catalytic domain. Integral membrane tyrosine  
kinases have been shown to mediate cellular signals  
important for growth and differentiation. The transduction  
of many extracellular signals to the cytoplasm occurs as a  
result of the binding of ligands such as growth factors,  
20 for example, to receptor tyrosine kinases at the cell  
surface. In most cases, ligand binding activates the  
cytoplasmic tyrosine kinase catalytic domain and culminates  
in tyrosine phosphorylation of multiple substrates in the  
cytoplasm.

25 Increased expression of membrane-spanning  
receptor tyrosine kinases frequently has been associated  
with alterations in normal cellular processes. The  
affected cellular processes include cell proliferation,  
differentiation and cancer, including, for example, human  
30 cancers. Specific examples of such cancers can include  
glioblastomas, squamous carcinomas and mammary carcinomas,  
which are associated with the amplification of the EGF  
receptor gene. Adenocarcinomas, breast cancers and gastric

cancers similarly are associated with aberrant expression of the HER2/neu receptor and certain breast carcinomas overexpress the erbB-3 gene, for example.

The correlation between aberrant expression and transforming ability also extends to members of the Eph subclass of receptor tyrosine kinases. For example, carcinomas of the liver, lung, breast and colon show elevated expression of Eph. Unlike many other tyrosine kinases, this elevated expression can occur in the absence of gene amplification or rearrangement. Such involvement of Eph in carcinogenesis also has been shown by the formation of foci of NIH 3T3 cells in soft agar and of tumors in nude mice following overexpression of Eph. Moreover, an antigen present on the surface of a pre-B cell leukemia cell line also has been identified as a member of the Eph subclass. Wicks et al., Proc. Natl. Acad. Sci., USA 89:1611-1615 (1992). This leukemia-specific marker, termed Hek, appears to be similar to the chicken Cek4 and mouse Mek4 of the Eph subclass of receptor tyrosine kinases (see Sajjadi et al., The New Biologist 3:769-778 (1991), which is incorporated herein by reference). As with Eph, Hek also was overexpressed in the absence of gene amplification or rearrangements in, for example, hemopoietic tumors and lymphoid tumor cell lines.

In addition to their roles in carcinogenesis, a number of transmembrane tyrosine kinases have been reported to play key roles during development. Examples include the mouse c-kit proto-oncogene and the *Drosophila* genes "sevenless" and "torso," which are involved in pattern formation. Consistent with this developmental role, many receptor tyrosine kinases other than those described above also have been shown to be developmentally regulated and predominantly expressed in embryonic tissues. Examples of these other tyrosine kinases include Cek1, which belongs to the FGF subclass, and the Cek4 and Cek5 tyrosine kinases

(Pasquale et al., Proc. Natl. Acad. Sci., USA 86:5449-5453 (1989); Sajjadi et al., *supra*, (1991); and Pasquale, E.B., Cell Reg. 2:523-534 (1991), all of which are incorporated herein by reference).

5 Eph was the first member of the Eph subclass of tyrosine kinases to be identified and characterized by molecular cloning (Hirai et al., Science 238:1717-1720 (1987)). The name Eph is derived from the name of the cell line from which the Eph cDNA was first isolated, the  
10 erythropoietin-producing human hepatocellular carcinoma cell line, ETL-1. The general structure of Eph is similar to that of other receptor tyrosine kinases and consists of an extracellular domain, a single membrane spanning region and a conserved tyrosine kinase catalytic domain. However,  
15 the structure of the extracellular domain of Eph, which comprises an immunoglobulin (Ig) domain at the amino terminus, followed by a cysteine-rich region and two fibronectin type III repeats in close proximity to the transmembrane domain, is completely distinct from that of  
20 previously described receptor tyrosine kinases. The juxtamembrane domain and carboxy-terminus regions of Eph also are unrelated to the corresponding regions of other tyrosine kinase receptors. Thus, the discovery of Eph defined a new subclass of receptor-type tyrosine kinases.

25 In addition to the isolation and characterization of Eph, other related tyrosine kinases now have been identified. Cek4 and Cek5 were identified by screening a chicken embryo cDNA expression library with anti-phosphotyrosine antibodies (Sajjadi et al., *supra*, (1991)  
30 and Pasquale, *supra*, (1991)). This method of identification was successful because Cek4 and Cek5 are expressed in embryonic tissues and have tyrosine kinase activity even when expressed as partial fragments in bacteria. Other Eph-related kinases that have been  
35 identified include Hek (Wicks et al., *supra*, (1992)), Sek

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(Gilardi-Hebenstreit et al, Oncogene 7:2499-2506 (1992)),  
Eck (Lindberg and Hunter, Mol. Cell. Biol. 10:6316-6324  
(1990)), Elk (Lhotak et al., Mol. Cell. Biol. 11:2496-2502  
(1991)) and Eek (Chan and Watt, Oncogene 6:1057-1061  
5 (1991)). These tyrosine kinases were cloned using a  
variety of methods.

The number of existing Eph-related kinases is not  
known and cannot be predicted. However, the Eph subclass  
already represents the largest known subclass of receptor  
10 tyrosine kinases, comprising at least 10 distinct members.  
The kinases belonging to the Eph subclass are so classified  
because each includes features such as the amino terminal  
Ig domain, the cysteine-rich stretch and two fibronectin  
type III repeats in the extracellular domain, which are  
15 conserved within the Eph subclass. However, despite these  
common structural features, the overall amino acid  
sequences outside the catalytic domain are quite different,  
indicating that different members of the Eph subclass  
interact with distinct ligands and substrates and, thus,  
20 exert distinct functions. This notion is supported by the  
differential distribution of different Eph-related kinases  
in adult tissues.

There is no indication whether other Eph-related  
kinases exist and, if so, what their relationship is to the  
25 known Eph-related kinases. Nevertheless, despite  
similarities among the Eph-related receptor tyrosine  
kinases, each is different and, as such, functions in  
related but distinct cellular processes. For example,  
many members of the Eph subclass are expressed in the  
30 nervous system during development and thus are likely to be  
involved in nerve regeneration processes. The aberrant  
expression or uncontrolled regulation of any one of these  
receptor tyrosine kinases can result in different  
malignancies and pathological disorders. Therefore, the  
35 identification and characterization of novel transmembrane

tyrosine kinases should provide important insights into the mechanisms underlying oncogenesis and cellular growth control pathways.

There thus exists a need to identify additional  
5 receptor tyrosine kinases and to manipulate them in order to diagnose pathological conditions and control cellular processes. The present invention satisfies this need and provides related advantages as well.

### SUMMARY

10 The invention is directed to substantially purified Eph-related protein tyrosine kinases, or functional fragments thereof, having about 23 to 66 percent amino acid sequence identity in their carboxyl terminal variable region compared to the other known members of the  
15 Eph subclass of tyrosine kinases. Nucleic acids encoding such Eph-related protein tyrosine kinases, vectors and host cells also are provided. The invention also is directed to a method of diagnosing cancer. The method includes removing a tissue or cell sample from a subject suspected  
20 of having cancer and determining the level of Eph-related protein tyrosine kinase in the sample, wherein a change in the level or activity of a Eph-related protein tyrosine kinase compared to a normal sample indicates the presence of a cancer or correlates with a specific prognosis.

### 25 BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows a comparison of the amino acid sequences from members of the Eph family. Dots replace residues in Cek4 (SEQ ID NO: 16), Cek6 (SEQ ID NO: 2), Cek7 (SEQ ID NO: 4), Cek8 (SEQ ID NO: 6), Cek9 (SEQ ID NO: 8),  
30 Cek10 (SEQ ID NO: 10), Eck and Eph that are identical to the corresponding residue in Cek5 (SEQ ID NO: 18). Dashes represent gaps introduced in the sequences to aid in the

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alignment. The insertion sequence of Cek5 also is presented (Cek5\*; SEQ ID NO: 12) and the insertion sequences of Cek7\* (SEQ ID NO: 20) and Cek10\* (SEQ ID NO: 14) are in parentheses. The conserved cysteines are indicated by the symbol " and the kinase domain is delimited by arrows. Open circles indicate the hydrophobic and aromatic residues that are conserved in the first fibronectin type III repeat and asterisks indicate the conserved residues of the second fibronectin type III repeat. The filled circle indicates the site of putative tyrosine autophosphorylation in the catalytic domain. The putative signal peptide sequences and transmembrane domains are underlined. Amino acids are numbered at the left of the sequences. The symbol + indicates the location of the extracellular domain amino acid insertion RICTPDVSGTVGSRPAADH (SEQ ID NO: 23), corresponding to Cek6 amino acids 426-444. Alignments were made by eye in the regions corresponding to Cek5 residues 1-615 and using the program DFALIGN (Feng and Doolittle, J. Mol. Evol., 25:351-360 (1987), which is incorporated herein by reference) in the regions corresponding to Cek5 residues 616-995.

Figure 2 shows a RNA blot analysis of Cek mRNAs. Polyadenylated chicken RNA from 10-day embryonic and adult tissues was hybridized with Cek-specific cDNA probes and with a chicken  $\beta$ -actin probe. Hybridization conditions were as described in Example I. The positions of RNA molecular weight standards (in kilobases, kb) are indicated on the right.  $\beta$ -actin transcripts are present in the ~2.0 kb size range.

Figure 3 shows a RNA blot analysis of Cek5 mRNAs. Polyadenylated RNA from body tissues (lanes 1 and 2) and brain (lanes 3 and 4) of 10-day chicken embryos was hybridized with a Cek5-specific cDNA (lanes 1 and 3). The same blots were then stripped and rehybridized with a 48 bp oligonucleotide antisense probe corresponding to the



juxtamembrane insertion sequence of Cek5 (lanes 2 and 4). Hybridization conditions were as described in Example I. The positions of RNA molecular weight standards (in kb) are indicated on the right.

5                    Figure 4 shows immunoblotting with antibodies to different Eph-related kinases. Fractions from 10-day embryonic brain containing either membrane-associated proteins (M) or soluble proteins (S) were probed with anti-Cek4 (4), anti-Cek8 (8,) or anti-Cek9 (9) antibodies.  
10 Equal amounts of protein were loaded in all the lanes. IP, immunoprecipitates from 11-day embryonic retina with anti-Cek8 antibodies (8) or with normal rabbit IgGs (Ig). The immunoprecipitates were then probed with anti-Cek8 antibodies.

15                    Figures 5.A. to 5.D. show the expression and tyrosine phosphorylation of Cek8 and Cek5 in transformed cell lines. Cell lysates were prepared from the rat central nervous system (CNS) tumor-derived cell lines B23, B28, B35, B49 and B50, the mouse embryonic carcinoma cell  
20 line, P19, and the human keratinocyte cell line HaCaT (Ha). Panels A and B show immunoprecipitates with anti-Cek8 antibodies. Panels C and D show immunoprecipitates with anti-Cek5 antibodies. The immunoprecipitation was followed by *in vitro* kinase reaction in the samples shown in panel  
25 C. The immunoblot in panel A was probed with anti-Cek8 antibodies. The immunoblots in panels B, C and D were probed with anti-phosphotyrosine antibodies.

                  Figures 6.A. to 6.F. demonstrate that Cek8 phosphorylation on tyrosine is increased in transformed  
30 cells and correlates with increased *in vitro* catalytic activity. Lysates from LMH cells and extracts of 10 day embryonic liver and adult liver were immunoprecipitated with anti-Cek8 antibodies, probed with anti-phosphotyrosine antibodies (panel A), then reprobed with anti-Cek8

antibodies (panel B). Lysates from normal chicken embryo fibroblasts and Rous sarcoma virus transformed chicken embryo fibroblasts were immunoprecipitated with anti-Cek8 antibodies, probed with anti-phosphotyrosine antibodies (panel C) and reprobed with anti-Cek8 antibodies (panel D).

Panels E and F show immunoblots of immunoprecipitated Cek8 (lane 1) or  $\beta$ -galactosidase-Cek4 fusion protein substrate (lanes 2-5). The fusion protein was phosphorylated for 1 min at 37 °C by Cek8 (lane 2), 1 min at 37 °C by tyrosine phosphorylated Cek8 (lane 3), 1 min at 0 °C by Cek8 (lane 4), 1 min at 0 °C by tyrosine phosphorylated Cek8 (lane 5). Immunoblots were probed with anti-phosphotyrosine antibodies (panel E) and reprobed with anti- $\beta$ -galactosidase antibodies (panel F).

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#### DETAILED DESCRIPTION OF THE INVENTION

The invention relates to the identification and characterization of seven novel members of the Eph subclass of membrane-spanning tyrosine kinases. The identification of these members doubles the number of kinases within this subclass, bringing the total to at least ten different Eph-related kinases. These Eph-related kinases therefore comprise the largest known subclass of integral membrane tyrosine kinases. The large number of different Eph-related kinases indicates that these receptors regulate a number of distinct cellular processes during development as well as in the adult organism. Therefore, identification of novel proteins within this subclass and isolation of their encoding nucleic acids allows the control of different cellular processes through the production of specific agonists and antagonists and through genetic therapy.

In one embodiment seven novel kinases of the Eph subclass of receptor protein tyrosine kinases have been

identified. The cDNAs encoding these Eph-related kinases were identified by hybridization at differential stringencies to identify distinct, but related receptor tyrosine kinases. All of the kinases exhibit gross structural features of known receptor tyrosine kinases in that they contain an extracellular ligand binding domain, a transmembrane domain and a cytoplasmic catalytic domain. These novel kinases are related to the Eph subclass of receptor tyrosine kinases and are designated Cek6 through 10 Cek10<sup>+</sup> (SEQ ID NOS: 1 to 14, and 19 to 22.) The overall sequence identity between these Eph-related kinases varies significantly with each of the novel Eph-related receptors being identified by its carboxyl terminal variable region.

In another embodiment, the novel Eph-related 15 kinases exhibit distinct tissue distribution patterns and developmental expression. Six of the kinases can be found to be expressed in both the embryonic brain and body tissues. The seventh Eph-related kinase, Cek5<sup>+</sup>, is expressed only in the embryonic brain. Indicative of their 20 roles in cellular processes, such as embryonic signal transduction pathways, these Eph-related kinases display distinct patterns of expression in adult tissues, including the neuronal specific expression of Cek5<sup>+</sup>. These distinct patterns can be used to diagnose aberrations in normal 25 cellular processes, such as those leading to uncontrolled malignant cell growth. For example, as described below, Cek8 activity is increased in various tumor cells as compared to normal cells. In addition to diagnosing such aberrations, it is also possible to treat defects caused by 30 the unregulated expression of Eph-related kinases through the use of gene therapy. Reagents affecting the expression or activity of Eph-related kinases can also be useful for inducing nerve regeneration following injury.

As used herein, the term "Eph-related protein 35 tyrosine kinase" or "Eph-related kinase" refers to a

receptor tyrosine kinase having an extracellular ligand binding domain, a transmembrane domain and a cytoplasmic catalytic domain, and belonging to the Eph subclass of receptor tyrosine kinases. Eph-related kinases include, for example, the receptor tyrosine kinases Cek6 (SEQ ID NO: 2), Cek7 (SEQ ID NO: 4), Cek7\* (SEQ ID NO: 20), Cek7' (SEQ ID NO: 22), Cek8 (SEQ ID NO: 6), Cek9 (SEQ ID NO: 8), Cek10 (SEQ ID NO: 10), Cek5\* (SEQ ID NO: 12) and Cek10\* (SEQ ID NO: 14). Such kinases exhibit an overall amino acid sequence identity to Eph of greater than about 40 percent. The extreme carboxyl terminal cytoplasmic regions of the kinases are not well conserved and can be used to differentiate among them. This extreme carboxyl terminal cytoplasmic region begins just after the catalytic domain at about residue number 900 and extends to the C-terminal most residue. Therefore, the term "carboxyl terminal variable region" as used herein, refers to this extreme C-terminal region of the sequence which is divergent between the different members of the Eph subclass of tyrosine kinases. The actual sequence identities between different kinases within the Eph subclass are as follows: Cek5-Cek10: 66%; Cek5-Cek6: 54%; Cek5-Cek9: 50%; Cek5-Cek8: 38%; Cek5-Cek7: 34%; Cek5-Cek4: 24%; Cek5-Eek: 39%; Cek5-Eck: 36%; Cek5-Eph: 33%; Cek10-Cek6: 64%; Cek10-Cek9: 56%; Cek10-Cek8: 47%; Cek10-Cek7: 45%; Cek10-Cek4: 32%; Cek10-Eek: 41%; Cek10-Eck: 39%; Cek10-Eph: 37%; Cek6-Cek9: 46%; Cek6-Cek8: 50%; Cek6-Cek7: 40%; Cek6-Cek4: 31%; Cek6-Eek: 39%; Cek6-Eck: 36%; Cek6-Eph: 32%; Cek9-Cek8: 46%; Cek9-Cek7: 47%; Cek9-Cek4: 29%; Cek9-Eek: 36%; Cek9-Eck: 33%; Cek9-Eph: 35%; Cek8-Cek7: 37%; Cek8-Cek4: 26%; Cek8-Eek: 39%; Cek8-Eck: 36%; Cek8-Eph: 30%; Cek7-Cek4: 36%; Cek7-Eek: 35%; Cek7-Eck: 43%; Cek7-Eph: 37%; Cek4-Eek: 29%; Cek4-Eck: 27%; Cek4-Eph: 23%; Eek-Eck: 26%; Eek-Eph: 32%; Eck-Eph: 52%. Therefore, the carboxyl terminal variable region exhibits an amino acid sequence identity of about 23 to 66 percent between the different Eph-related kinases. The novel Eph-related kinases described herein fall within

this level of sequence divergence and can therefore be distinguished by comparison to the known members of the Eph subclass. Known members of this subclass include, for example, Eph, Cek4, Cek5, Mek4, Hek, Sek (or mouse Cek8),  
5 Eck, Elk (or rat Cek6) and Eek.

It is understood that limited modifications may be made without destroying biological functions of Eph-related kinases and that only a portion of the entire primary structure may be required in order to effect a  
10 particular activity. Such biological functions and activities can include, for example, signal transduction, ligand binding and/or tyrosine kinase activity. For example, the Eph-related kinases of the invention have amino acid sequences substantially similar to those shown  
15 for Cek7, Cek7\*, Cek7', Cek9, Cek10, Cek5\*, Cek10\* and chicken Cek6 and Cek8 in Figure 1 (hereinafter referred to as Cek6 through Cek10\*), but minor modifications of these sequences which do not destroy their activity also fall within the definition of Eph-related kinases and within the  
20 definition of the protein claimed as such. Moreover, fragments of the sequences of Cek6 through Cek10\* in Figure 1 (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 20 and 22), which retain the function of the entire protein as well as functional domains that contain at least one function of  
25 the intact protein are included within the definition. Functional domains can include, for example, active ligand binding and catalytic domains. The boundaries of such domains are not important so long as activity is maintained. It is also understood that minor modifications  
30 of the primary amino acid sequence can result in proteins which have substantially equivalent or enhanced function as compared to the sequences set forth in Figure 1 (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 20 and 22). These modifications may be deliberate, as through site-directed  
35 mutagenesis, or may be accidental such as through mutation in hosts which produce Eph-related kinases. All of these

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modifications are included as long as biological function is retained. Further, various molecules can be attached to Eph-related kinases, for example, other proteins, carbohydrates, or lipids. Cek8 (SEQ ID NO: 6), for example, can contain complex N-linked oligosaccharides (see below). Such modifications are included within the definition of Eph-related tyrosine kinase.

The term "substantially purified," when used to describe the state of Eph-related tyrosine kinases denotes the protein free of a portion of the other proteins and molecules normally associated with or occurring with Eph-related kinases in their native environment. Such substantially purified Eph-related kinases can be derived from natural sources, recombinantly expressed or synthesized by *in vitro* methods so long as some portion of normally associated molecules is absent.

"Isolated" when used to describe the state of the nucleic acids encoding Eph-related tyrosine kinases denotes the nucleic acids free of at least a portion of the molecules associated with or occurring with Eph-related nucleic acids in the native environment.

As used herein, the term "vector" includes nucleic acids that are capable of harboring a natural or recombinant DNA sequence of interest. Vectors are usually derived from, or contain some sequences from, a natural source. For example, bacteriophage vectors containing specially engineered features that are largely derived from the phage's genome and are capable of carrying out some part of its infectious cycle. On the other hand, the sequences contained within plasmids are usually derived from different sources and compiled into a single molecule to carry out specific tasks. Thus, there are many different types of vectors and each is used according to the need to perform a desired function. Functions can include, for

example, propagation in a desired host, cloning recombinant or natural fragments of DNA, mutagenesis, expression and the like. In sum, "vector" is given a operative definition, and any DNA sequence which is capable of effecting a function of a specified DNA sequence disposed therein is included in this term as it is applied to the specified sequence.

The invention provides a substantially purified Eph-related protein tyrosine kinase, or functional fragment thereof. Also provided is a substantially purified chicken Eph-related protein tyrosine kinase. The substantially purified Eph-related protein tyrosine kinase exhibits about 23 to 66 percent amino acid sequence identity in its carboxyl terminal variable region compared to known members of the Eph subclass of tyrosine kinases. The amino acid sequences are substantially the same as that shown for Cek6 through Cek10<sup>+</sup> in Figure 1 (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 20 and 22.)

The invention also provides an isolated nucleic acid encoding a Eph-related protein tyrosine kinase, or functional fragment thereof. The isolated nucleic acid encoding a Eph-related protein tyrosine kinase exhibits about 23 to 66 percent amino acid sequence identity in its carboxyl terminal variable region compared to known members of the Eph subclass of tyrosine kinases. The encoding nucleotide sequences are substantially the same as that shown for Cek6 (SEQ ID NO: 1), Cek7 (SEQ ID NO: 3), Cek8 (SEQ ID NO: 5), Cek9 (SEQ ID NO: 7), Cek10 (SEQ ID NO: 9), Cek5<sup>+</sup> (SEQ ID NO: 11), Cek10<sup>+</sup> (SEQ ID NO: 13), Cek7<sup>+</sup> (SEQ ID NO: 19) and Cek7' (SEQ ID NO: 21) (hereinafter Cek6 through Cek10<sup>+</sup>).

The isolation of seven cDNAs that encode novel Eph-related receptor tyrosine kinases is disclosed herein. The predicted amino acid sequences of these Eph-related

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kinases are shown in Figure 1 along with other known Cck kinase sequences and those of Eph and Eck. A number of conserved features serve to define the newly discovered kinases as members of the Eph subclass. These include an amino terminal immunoglobulin domain followed by a cysteine-rich stretch in the extracellular domain, with the position of most cysteines conserved, and sequences corresponding to two fibronectin type III repeats in close proximity to the transmembrane domain (O'Bryan et al., Mol. Cell. Biol. 11:5016-5031 (1991) and Pasquale, *supra*, (1991), the former of which is incorporated herein by reference). Potential sites of N-glycosylation are primarily localized in the C-terminal half of the extracellular regions. The homologies in the extracellular domains indicates that the different members of the Eph family can bind a similar class of ligands. Figure 1 also shows that the Eph family, with the inclusion of the new members that have been identified, can now be considered the largest known family of membrane-spanning tyrosine kinases. Such a large number of tyrosine kinases in this one class is surprising in view of the fact that the other families of receptor tyrosine kinases have fewer members.

The catalytic domains of the Eph-related kinases are highly conserved and exhibit amino acid identities ranging between 61% and 90%. The C-terminal tails are less conserved (Figure 1) and therefore constitute a variable region which can be used to specify the distinct Eph-related kinases. Only one of the tyrosines in the C-terminal variable region, corresponding to tyrosine 939 of Cck5, is conserved in all the members of the Eph family, with the exception of Cck4. This conserved tyrosine residue represents a likely site of autophosphorylation and regulation, Ullrich and Schlessinger, Cell 61:203-212 (1990). The large size of the Eph subclass of receptor tyrosine kinases, the variability within their sequences and their different tissue distributions indicate that each



receptor can, for example, serve distinct functions during cellular processes.

The variability in both the lengths and sequences of the juxtamembrane domains observed in the Eph-related  
5 kinases is unusual among tyrosine kinases belonging to the same subclass, Ullrich et al., *supra*, 1990. Because clones encoding variants with amino acid insertions in the juxtamembrane domain were isolated for Cek5, Cek7 and Cek10, the variability in the lengths of the juxtamembrane  
10 domains is likely to originate by alternative splicing (Figure 1). Juxtamembrane domains are important for the modulation of receptor functions by heterologous stimuli, for example, through phosphorylation by other kinases. The juxtamembrane domains of the members of the Eph family  
15 contain numerous serines, threonines and tyrosines that can serve as sites of regulation by phosphorylation, Kemp et al., Trends Biol. Sci. 15:342-346 (1990), which is incorporated herein by reference. For example, Cek9 and Cek10, as well as Cek5, Cek6, and Eck contain the consensus  
20 sequence (S/T)P, which is recognized by proline-dependent protein kinases such as cdc2, Kemp et al., *supra*, (1990). Juxtamembrane domains have also been indicated to be important in the regulation of the subcellular distribution of the kinase and in the binding of some substrates  
25 (Ullrich et al., *supra*, 1990).

The mRNA corresponding to Cek5\* (SEQ ID NO: 11), the variant form of Cek5, was shown to be specifically expressed in the CNS, indicating that Cek5\* functions primarily in neuronal cellular functions. Indicative of  
30 this is another tyrosine kinase, src, which has been shown to encode neuronal specific variants containing 6 to 17 amino acid insertions in the regulatory (non-catalytic) region (Brugge et al., Nature 316:554-557 (1985); Martinez et al., Science 237:411-415 (1987); Pyper et al., Mol.  
35 Cell. Biol. 10:2035-2040 (1990), all of which are

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incorporated herein by reference). These neuronal forms of c-src have higher specific catalytic activity than non-neuronal c-src.

Although the predicted molecular masses of the  
5 different members of the Eph family are similar, the sizes of their transcripts appear quite varied (4 to 10 kb). In addition, several mRNA species for each of the Eph-related kinases, particularly in the CNS, were detected using a panel of probes. As described below, the patterns of  
10 expression of these novel Eph-related kinases are also distinct.

DNA sequences encoding the polypeptides of Eph-related kinases can be obtained by methods known to one skilled in the art. The sequences described herein are  
15 sufficient for one skilled in the art to practice the invention. Such methods include, for example, cDNA synthesis and polymerase chain reaction (PCR). The need will determine which method or combination of methods is to be used to obtain the desired sequence. Expression can be  
20 performed in any compatible vector/host system. Such systems include, for example, plasmids or phagemids in procaryotes such as *E. coli*, yeast systems and other eucaryotic systems such as mammalian cells. Additionally, the Eph-related kinases can also be expressed in soluble or  
25 secreted form depending on the need and the vector/host system employed.

Such vectors and vector/host systems are known, or can be constructed by those skilled in the art and should contain all expression elements necessary for the  
30 transcription, translation, regulation, and sorting of the polypeptide which makes up the Eph-related kinase. Other beneficial characteristics may also be contained within the vectors such as mechanisms for recovery of the nucleic acids in a different form. Phagemids are a specific

example of this because they can be used either as plasmids or as bacteriophage vectors. The vectors can also be for use in either procaryotic or eucaryotic host systems so long as the expression elements are of a compatible origin.

5 One of ordinary skill in the art will know which host systems are compatible with a particular vector. Thus, the invention provides vectors, host cells transformed with the vectors and Eph-related kinases produced from the host cells containing a nucleic acid encoding a Eph-related

10 kinase.

The invention also provides methods of diagnosing cancer and determining cancer prognosis. The method includes removing a tissue or cell sample from a subject suspected of having cancer and determining the level of

15 Eph-related protein tyrosine kinase in said sample, wherein a change in the level or activity of a Eph-related protein tyrosine kinase compared to a normal sample indicates the presence of a cancer or indicates the level of malignancy of a cancer and, therefore, the most appropriate course of

20 treatment.

As stated previously, receptor tyrosine kinases are involved in many signal transduction events that regulate important cellular processes. Such processes include, for example, cellular differentiation and

25 proliferation. Abnormal regulation or expression of the signal transduction machinery can lead to aberrant and malignant growth of the abnormally regulated cells. Abnormal expression of Eph is known to be associated with carcinomas of the liver, lung, breast and colon, for

30 example. Likewise, since some Eph-related tyrosine kinases are, at least, found within the same tissues as Eph, their abnormal expression may also lead to the development of the carcinomas described above as well as other types of cancers. For example, increased Cck8 activity was found in

35 embryonal carcinoma cells and a keratinocyte tumor cell

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line (see Example II). Additionally, cancers of the neuronal lineage are likely to be caused by the abnormal expression or regulation of an Eph-related kinase such as Cek8 (see Example II) or Cek5<sup>+</sup> since this Eph-related kinase  
5 is found exclusively in neuronal tissues. Cek5<sup>+</sup>, Cek5 and the other Eph-related kinases expressed in the nervous system also are likely to be involved in nerve regeneration.

The important role that these receptor tyrosine  
10 kinases play in cellular processes can be advantageously used to diagnose early stages of cancer within a cell sample or tissue. A change in the amount or activity of an Eph-related kinase in a suspected sample, compared to a normal sample, will be indicative of cancerous stages and  
15 of their level of malignancy. Depending on whether the normal state is caused by the presence or absence of an Eph-related kinase, the change can involve either an increase or decrease in the amount or activity of the Eph-related kinase. For example, Cek8 activity is increased in  
20 various tumor cells (see Example II). Thus, increased activity of an Eph-related kinase of the invention such as Cek8 (SEQ ID NO: 6) can be useful for identifying the presence of transformed cells such as occur in a cancer.

One skilled in the art can measure the level or  
25 activity of an Eph-related kinase, for example, in a tissue sample obtained from a subject suspected of having a cancer or a developmental abnormality and the level or activity of the Eph-related kinase can be compared to the level or activity known to be present in a normal sample. Such a  
30 known level of activity can be determined by obtaining a significant number of tissue samples from subjects that do not have a cancer or a developmental abnormality and measuring the levels or activities of an Eph-related kinase in the population of samples. Methods for determining the  
35 level or activity of Eph-related kinases are known to the

skilled artisan and include, for example, RNA and protein blot analysis, ELISA using specific antibodies to each of the Eph-related kinases and direct measurement of catalytic activity such as tyrosine kinase activity. Such methods are described in detail in Example II or are otherwise known in the art (see, for example, Harlow et al., Antibodies: A Laboratory Manual Cold Spring Harbor Laboratory (1988), which is incorporated herein by reference).

The following examples are intended to illustrate, but not limit the invention.

#### EXAMPLE I

##### Isolation and Characterization of Eph-Related Tyrosine Kinases

This example shows the cloning and sequencing of the Eph-related kinases Cek6 through Cek10'. Structural characteristics and patterns of expression are also described.

To find novel members of the Eph family, various cDNA probes were used at different stringencies to screen a 10 day embryonic library as well as a 13 day embryonic brain cDNA library. The probes were derived from Cek4 (SEQ ID NO: 15) or Cek5 (SEQ ID NO: 17), which had been previously isolated based on phosphotyrosine content. Following subcloning and sequence analysis, it was found that the newly isolated cDNA clones encoded seven different Eph-related tyrosine kinases. Their isolation and structure are described below.

Briefly, a 10-day chicken embryo  $\lambda$ gt11 cDNA library (Clontech) and a 13-day embryonic brain  $\lambda$ gt11 cDNA library were used to isolate the cDNA clones. Screening was performed at different stringencies using the following procedure. Plaques were transferred to nylon membranes

(Micron Separations Inc.) on duplicate filters and hybridized to the appropriate probes at one of two stringencies (50% formamide, 42°C; or 50% formamide, 37°C). Conditions used were those recommended by the manufacturer and probes were detected using a nonradioactive DNA labeling and detection method (Boehringer Mannheim). Plaques identified as positive were subjected to three rounds of purification prior to DNA extraction using Lambda-TRAP (Clontech). Inserts from recombinant lambda DNA were subcloned in pBluescript vectors (Stratagene, San Diego, CA) using standard procedures and the sequences were analyzed on both strands, using the dideoxynucleotide chain-termination technique with Sequenase (United States Biochemical, Cleveland, OH).

Several clones distinguishable over known Eph tyrosine kinases were isolated using the Cek5 probe, which corresponded to nucleotides 495-3223 (Pasquale, *supra*, (1991)). The clones include: one Cek5<sup>+</sup> cDNA clone (from the chick embryo library); three Cek6 clones (two from the embryonic brain and one from the chick embryo library); one Cek7 clone (from the chick embryo library); one Cek7<sup>+</sup> clone (from the chick embryo library); one Cek7' clone (from the embryonic brain library); one Cek9 clone (from the chick embryo library); one Cek10<sup>+</sup> clone (from the chick embryo library) and two Cek10 or Cek10<sup>+</sup> clones, which are indistinguishable because they do not encode the juxtamembrane domain, (one from the chick embryo and one from the embryonic brain library).

A Cek4 probe (corresponding to nucleotides 748-1756; see Sajjadi et al., *supra*, 1991), on the other hand, was used to isolate one Cek8 clone (from the chick embryo library). Also, following its initial isolation, a Cek10 probe, corresponding to residues 400-596 in Figure 2, was used to isolate clones extending further into the 5' end

from the chick embryo library. Of the two clones isolated, one represented Cek10 and one Cek10\*.

The above-identified Eph-related kinases were characterized in terms of tissue distribution and expression by RNA blot analysis. Poly-A<sup>+</sup> RNA was prepared from chicken tissues using the procedure of Badley et al., Biotechniques 6:114-116 (1988), which is incorporated herein by reference. Poly-A<sup>+</sup> RNA (4-5  $\mu$ g) was size-fractionated alongside RNA molecular weight markers on 0.9% agarose gels containing formaldehyde (Sambrook et al., Molecular Cloning: A Laboratory Manual (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989), which is incorporated herein by reference) and transferred to nitrocellulose filters (Schleicher & Schuell) according to methods known to one skilled in the art. The membranes were prehybridized for 2 hours and then hybridized under stringent conditions (50% formamide, 5x SSPE, 5x Denhardt's reagent, 0.5% SDS, 100  $\mu$ g/ml salmon testes DNA, 42°C). Probes were labeled with <sup>32</sup>P dATP by the random-primed method of Feinberg and Vogelstein, Anal. Biochem. 132:6-13 (1983), which is incorporated herein by reference. T4 polynucleotide kinase was used to label the 5' end of the Cek5\* specific oligonucleotide (Sambrook et al., *supra*, 1989). Filters were washed to a final stringency of 0.1x SSPE, 0.1% SDS at 58°C prior to exposure to Kodak XAR-5 X-ray film. For autoradiography of  $\beta$ -actin controls, intensifying screens were typically omitted and exposure time was reduced to 2 hours.

The following cDNA probes were used for RNA blot analysis: Cek4, 1.2 kb, same probe used for the library screening described previously, hybridizes to the region encoding amino acid residues 240-575; Cek5 probe, 1.2 kb, hybridizes to the 3' untranslated region; Cek6 5' probe, 1.3 kb, hybridizes to amino acid residues 1-438; Cek6 3' probe, 0.6 kb, hybridizes to the region following amino

acid 844; Cek7 5' probe, 0.4 kb, hybridizes to amino acid residues 1-136; Cek7 3' probe, 2.0 kb, hybridizes to the region following amino acid 137, including the 3' untranslated region; Cek8 probe, 1.2 kb, hybridizes to the region encoding amino acid residues 1-406; Cek9 probe, 0.6 kb, hybridizes to the region encoding amino acid residues 1-208; Cek10 probe, 0.6 kb, hybridizes to the region encoding the 10 C-terminal amino acids and to about 600 nucleotides of 3' untranslated region. For Cek6 and Cek7, the 3' Cek6 probe and the 5' Cek7 probe were used for the embryonic tissues mRNAs and a mixture of 5' and 3' probes for the adult tissues mRNAs.

Polyadenylated RNA was isolated from a number of adult chick tissues, as well as from brain and body tissues of 10-day embryos. These RNAs were then used for RNA blot analysis using the above specific probes. Probes were designed to minimize the possibility of cross-hybridization among the related kinases. Chicken  $\beta$ -actin DNA was used as a control probe (Cleveland et al., Cell 20:95-105 (1980), which is incorporated herein by reference).

The amino acid sequence of Cek4 (SEQ ID NO: 16) is 67% identical to that of Cek5 (SEQ ID NO: 18) in the catalytic and C-terminal regions and is most closely related to that of Cek7 (SEQ ID NO: 4) (75% amino acid identity in the same regions) (Figure 1). Preliminary data had indicated that Cek4 was highly expressed in the chicken developing brain and embryonic tissues, but no information was obtained on the adult pattern of expression in the chick. These data were therefore included in Figure 2. The 7.5 kb Cek4 transcript previously described was confirmed to be abundant in 10 day embryonic tissues. Expression was pronounced in the adult brain and retina, and lower but detectable in all other adult tissues examined, except the liver. In addition to the major 7.5 kb transcript, a smaller Cek4 transcript (of about 5 kb)



was found to be expressed at lower levels in the adult brain.

The Cek6 amino acid sequence (SEQ ID NO: 2) is most closely related to that of rat Elk (96% identity in the catalytic and C-terminal regions). Of the Cek members of the Eph subclass, Cek6 is most closely related to Cek5 (SEQ ID NO: 18) and Cek10 (SEQ ID NO: 10) (82% amino acid identity with both, in the catalytic and C-terminal regions) (Figure 1). The two Cek6 cDNAs that were isolated from a 13-day chick embryo brain library were identical and both encoded a protein with a deletion of 32 amino acids and an insertion of 19 amino acids in the extracellular region (Figure 1). However, these may be cloning artifacts, particularly the deletion, since it causes a shift in the reading frame and the premature termination of the encoded protein. A 4.4 kb Cek6 transcript was found to be expressed at high levels in the 10-days embryo and in adult brain, lung, heart and skeletal muscle (Figure 2). Low levels of Cek6 expression were detected in all other adult tissues tested. A second larger Cek6 transcript of about 6.5 kb was detected at low levels in the adult brain.

The amino acid sequence of Cek7 (SEQ ID NO: 4) is 71% identical to that of Cek5 (SEQ ID NO: 18) in the catalytic and C-terminal regions and is most closely related to those of Cek4 (SEQ ID NO: 16) and Cek9 (SEQ ID NO: 8) (75% amino acid identity with both, in the same regions) (Figure 1). A variant form of Cek7, containing a 22 amino acid insertion in the juxtamembrane domain (Figure 1) also was isolated and designated Cek7\*. Cek7 (SEQ ID NO: 4) and Cek7\* (SEQ ID NO: 20) may originate from the same gene by alternative splicing. A second variant form of Cek7, designated Cek7' (SEQ ID NO: 22), which also presumably originates via alternative splicing, differs from Cek7 in the C-terminal 33 amino acids. Cek7 appears to have the lowest levels of expression among all the Eph

related kinases examined. Three different transcripts of about 4.4 kb, 7 kb and 8.5 kb were detected in the 10-day embryonic brain. Expression was weaker in the rest of the 10-day embryo, where only the 4.4 kb transcript could be  
5 detected (Figure 2). Cek7 transcripts were not detected in the adult tissues, except for a barely detectable 8.5 kb transcript in the brain (Figure 2).

Cek8 (SEQ ID NO: 6) is equally related to Cek5 (SEQ ID NO: 18), Cek6 (SEQ ID NO: 2), Cek7 (SEQ ID NO: 4)  
10 and Cek10 (SEQ ID NO: 10) (74% amino acid identity in the catalytic and C-terminal regions) (Figure 1). A single 6 kb Cek8 transcript was found to be present in both the 10-day embryonic brain and body tissues (Figure 2). Cek8 (SEQ ID NO: 6) expression appears to be the highest in adult  
15 brain and retina and is also detectable in kidney, lung, skeletal muscle and thymus (Figure 2; see, also, Example II). Cek8 expression was not detected in heart and liver.

Cek9 (SEQ ID NO: 8) is most closely related to Cek5 (SEQ ID NO: 18) (77% identity at the amino acid level  
20 in the catalytic and C-terminal regions) (Figure 1). A 4.4 kb Cek9 transcript is present in embryonic brain and body tissues. Two additional and very minor transcripts of about 5.5 kb and 6.5 kb were detected exclusively in the 10-day embryonic brain (Figure 2). Among the adult tissues  
25 examined, Cek9 expression is prominent in the thymus and detectable in brain, retina, kidney, lung and heart. None of the other kinases examined displays such an elevated level of expression in the thymus. Cek9 expression was not detected in skeletal muscle and liver.

30 Cek10 (SEQ ID NO: 10) is most closely related to Cek5 (SEQ ID NO: 18) and Cek6 (SEQ ID NO: 2) (84% amino acid identity with both in the catalytic and C-terminal regions) (Figure 1). A variant form of Cek10, containing a 15 amino acid insertion in the juxtamembrane domain

(Figure 1), was also isolated and designated Cek10<sup>+</sup> (SEQ ID NO: 14). Cek10 and Cek10<sup>+</sup> may originate from the same gene by alternative splicing. Northern blot analysis identified two Cek10 transcripts of about 4.4 kb and 6 kb, present at  
5 different relative levels in 10-day embryonic brain and body tissues as well as in a number of adult tissues (Figure 2). Among the adult tissues examined, Cek10 expression was particularly prominent in the kidney. Lower  
10 detectable transcripts were also present in brain, liver, heart, skeletal muscle and thymus.

A variant form of Cek5, containing a 16 amino acid insertion in the juxtamembrane domain, was also identified and termed Cek5<sup>+</sup> (SEQ ID NO: 12) (Figure 1).  
15 This Cek5 variant may originate as a result of alternative splicing. With a Cek5 DNA probe recognizing both Cek5 and Cek5<sup>+</sup> (see Material and Methods), a 4.4 kb transcript was detected in both 10-day embryonic brain and body tissues (Figure 3, lanes 1 and 3). In addition, a much larger  
20 transcript (of about 10 kb) was detected in the 10-day embryonic brain (Figure 3, lane 3). Consistently with the previously reported expression of the Cek5 protein, Cek5 transcripts are more abundant in the brain than in other 10-day embryonic tissues. Using a probe corresponding to  
25 the 16 amino insertion in the juxtamembrane domain (Figure 3, lanes 2 and 4), Cek5<sup>+</sup> was found to be exclusively expressed in the CNS and only as the 4.4 kb transcript. Because Cek5 immunoreactivity in the CNS has been previously found to be confined to neurons, Cek5<sup>+</sup> appears to  
30 be a neuronal specific variant of Cek5.

Polyclonal antibodies recognizing specifically Cek4, Cek8 and Cek9 have been obtained and will be used for the characterization of these kinases (see Example II). Peptides corresponding to the carboxy-terminal ends of  
35 Cek4, Cek8 and Cek9 were coupled to bovine serum albumin

(BSA) with m-maleimido benzoyl-N-hydroxysuccinimide ester (Cek4) or with glutaraldehyde (Cek8 and Cek9) and used as immunogens. The peptides used were the following: Cek4, CLEHTKNSPVPV (SEQ ID NO 24); Cek8, KMQQMHGRMVPV (SEQ ID NO 25) and Cek9, KVHLNQLEPVEV (SEQ ID NO 26). The carboxy-terminal regions were chosen because they are poorly conserved within the Eph subclass, increasing the likelihood of obtaining antibodies specific for each kinase.

10           The antibodies were purified from the antiserum by affinity-chromatography on the appropriate peptides coupled to N-hydroxy-succinimide-activated agarose (BioRad). As shown in Figure 4, after affinity purification the antibodies to Cek4, Cek8 and Cek9  
15 recognize a single band of the expected apparent molecular mass (about 120 kiloDalton, kDa) in membranes-containing fractions isolated from 10-day embryonic brain, but not in fractions containing soluble proteins. These antibodies do not cross-react significantly with related members of the  
20 Eph subclass (not shown) and can be used for different applications such as immunoblotting, immunofluorescence microscopy and immunoprecipitation (see Figure 4). All of the antibodies are capable of immunoprecipitating the kinases from tissue extracts and, as expected, the  
25 immunoprecipitated kinases undergo *in vitro* autophosphorylation in the presence of ATP (see Example II).

          These techniques will allow the characterization of the kinases of the Eph subclass at the protein level.  
30 Coupled to a solid support, the antibodies can also be used to purify the kinases from tissues and cell lines. In the cases tested, antibodies generated to the chicken Eph-related kinases recognize the corresponding mammalian homologues. Thus, these antibodies could be used, for

example, to screen tumor samples for the presence of the appropriate Eph-related kinases.

## EXAMPLE II

### CHARACTERIZATION OF CEK8

5                   This example describes structural and functional characteristics of the Cek8 protein (SEQ ID NO: 6), including the expression and activity of Cek8 during development and in tumor cells.

#### A. Antibody preparation:

10                   Cek8 expression and activity was examined using immunological and immunohistochemical methods. An antigen for raising anti-Cek8 antibodies was prepared by coupling the peptide KMQQMHGRMVPV (SEQ ID NO: 25), which consists of the eleven carboxy terminal amino acids of Cek8, including  
15 an additional N-terminal lysine, to BSA using glutaraldehyde (Harlow and Lane, *supra*, 1988). An antigen for raising anti-Cek4 antibodies was prepared by coupling the peptide CLEHTKNSPVPV (SEQ ID NO: 24), which corresponds to the 12 carboxy terminal amino acids of Cek4,  
20 including an additional cysteine at the N-terminus, to BSA using m-maleimidobenzoyl-N-hydroxysuccinimide ester (Harlow and Lane, *supra*, 1988). Anti-Cek5 antibodies and anti-phosphotyrosine antibodies were prepared as described by Pasquale, *supra*, (1991). Antisera were raised in  
25 rabbits using standard methods (see, for example, Harlow and Lane, *supra*, 1988). The peptide antigen was coupled to N-hydroxy-succinimide-activated agarose and specific antisera were affinity purified.

#### B. Structural characterization of Cek8:

30                   Cek8 was immunoprecipitated and examined by immunoblotting as described in Section C.1., below. The

affinity purified anti-Cek8 antibodies recognized a protein having an apparent molecular mass of about 120 kDa, which was the expected size for Cek8. The calculated molecular mass of Cek8, however, is less than the 120 kDa observed by SDS-PAGE. Since Cek8 contains three consensus sites of N-linked glycosylation, Cek8 was examined for such glycosylation. When chicken embryo fibroblasts were grown in the presence of 1.6  $\mu\text{g/ml}$  tunicamycin, which inhibits N-linked glycosylation, the apparent molecular mass of Cek8 decreased by about 10 kDa.

In order to characterize the carbohydrate moiety of Cek8, lectin affinity chromatography was performed. Ten day embryonic chicken brains were sonicated in 10 ml PBS containing protease inhibitors (protease inhibitors are 1 mM phenylmethylsulfonyl fluoride, 0.2 trypsin inhibitor units aprotinin/ml, 10  $\mu\text{g/ml}$  pepstatin and 10  $\mu\text{g/ml}$  leupeptin and 1 mM sodium orthovanadate, a phosphatase inhibitor. The sonicated material was centrifuged at 2000 x g for 5 min to remove insoluble material, then the supernatant was centrifuged at 200,000 x g for 40 min.

The pellet, which contained the membrane enriched fraction, was solubilized in PBS containing 0.1% Triton X-100. The solubilized sample was centrifuged 5 min in a microfuge and the supernatant was collected. The extract was dialyzed overnight at 4 °C against 10 mM Tris-HCl, pH 7.4, loaded onto various lectin columns, including concanavalin A, lentil lectin, wheat germ agglutinin, ricin I lectin, peanut lectin or *Ulex europaeus* I lectin (EY Laboratories, Inc.; San Mateo CA), and the columns were eluted with 0.1 M methyl  $\alpha$ -D-mannopyranoside, 0.1 M D-mannose, 0.1 M N-acetyl-D-glucosamine, 0.1 M  $\alpha$ -lactose, 0.1 M  $\alpha$ -lactose or 0.05 M  $\alpha$ -L-fucose, respectively. Fractions were collected and analyzed by immunoblotting for the presence of Cek8 as described below.

Cek8 bound to the concanavalin A, lentil lectin, ricin I and wheat germ agglutinin columns and was eluted with the appropriate buffers. These lectins preferentially recognize N-linked sugar chains. Thus, this result is in agreement with the observed inhibition of glycosylation by tunicamycin. In contrast, Cek8 does not bind to peanut lectin, which primarily recognizes O-linked chains.

Binding to concanavalin A and elution with the relatively low concentration of 0.1 M methyl  $\alpha$ -D-mannopyranoside indicates that Cek8 contains biantennary complex type sugar chains (Osawa and Tsuji, Ann. Rev. Biochem. 56:21-42 (1987)). Binding to lentil lectin indicates that a fucose residue is present on the innermost N-acetylglucosamine residue in an oligosaccharide core. However, since Cek8 does not bind with *Ulex europaeus* I lectin, terminal fucose residues are not likely present (Sugii and Kabat, Carb. Res. 99:99-101 (1982)). Binding of Cek8 to wheat germ agglutinin indicates that sialic acid is present and binding to the ricin I column indicates that terminal  $\beta$ -galactosyl residues are present in complex sugar chains. These carbohydrate structures likely are located in the extracellular regions of Cek8 and can participate in interactions with extracellular molecules. *In vivo* phosphorylation on tyrosine of Cek8 can be achieved by exposing cells expressing Cek8 to wheat germ agglutinin.

### C. Expression and Catalytic Activity of Cek8:

This section describes the methods for determining Cek8 expression and activity in various tissues during development and in tumor cells.

#### 30 1. Methods

Cek8 expression and activity were determined by immunoprecipitation and immunoblot experiments. Cells from

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90% confluent tissue culture plates were washed 3x with ice cold phosphate buffered saline (PBS), collected in cold RIPA buffer (150 mM sodium chloride, 10 mM sodium phosphate, pH 7.2, 1% deoxycholate, 1% Triton X-100, 0.1% SDS) containing protease inhibitors, and lysed by sonication. Phosphotyrosine was added to a final concentration of 8 mM when immunoblotting was performed using anti-phosphotyrosine antibodies.

Tissues were removed from adult chickens or chicken embryos and sonicated in PBS containing protease inhibitors. Whole embryos were collected and sonicated in PBS. Lysates were stored at -70 °C. Protein concentrations were determined using a Bio-Rad protein assay (Bio-Rad Laboratories; Richmond CA). For immunoprecipitations, tissue extracts were diluted in RIPA buffer. Cell lysates and tissue extracts in RIPA buffer were precleared using Staph A (Boehringer-Mannheim; Indianapolis IN) as described by Pasquale (*supra*. 1991). The samples then were incubated 40 min with 20 µg anti-Cek4, anti-Cek5 or anti-Cek8 antibodies or 20 µg control rabbit IgG preabsorbed to 20 µl Staph A. The amount of antibody was selected to ensure that all of the antigen in the extracts or lysates was precipitated.

Immunoprecipitated material was washed 3x with RIPA buffer and 1x with PBS. Sample buffer was added, the immunoprecipitates were boiled for 5 min, separated by SDS-PAGE on 7.5% gels and transferred to nitrocellulose as described by Towbin et al., Proc. Natl. Acad. Sci., USA 76:4350-4354 (1979), which is incorporated herein by reference. Following transfer, the filters were incubated overnight in Tris-hydroxyethylaminoethane-buffered saline (TBS) containing 3% BSA, then incubated 4 hr in 3% BSA containing 3 µg/ml anti-Cek4, anti-Cek5, anti-Cek8 or anti-phosphotyrosine antibody. The filters were rinsed with TBS, then incubated for 1 hr with 0.2 µg/ml protein A



peroxidase (Sigma; St. Louis MO) in TBS containing 3% BSA. The filters were rinsed several times with TBS and developed using enhanced chemiluminescence reagents (Amersham; Arlington Heights IL). In some experiments, after detection, the filters were dried for a few hours, then incubated in 3% BSA in TBS and probed with a different antibody.

*In vitro* phosphorylation was performed as described by Pasquale, *supra*, (1991). Briefly, Cek8 was immunoprecipitated from 10 day embryonic brain extracts or from cell lysates. In control experiments, Cek5 was immunoprecipitated. Immunoprecipitations were performed as described above. The immune complexes were incubated for 30 min at 37 °C in phosphorylation buffer (25 mM N-2-hydroxyethylpiperazine-N'-2-ethanesulfonic acid, pH 7.5, 10 mM MgCl<sub>2</sub>, 10 mM MnCl<sub>2</sub>, 1 mM sodium orthovanadate, 0.1% Triton X-100, 150 μM ATP). Sample buffer was added and electrophoresis and transfer to nitrocellulose were performed as described above. Following transfer, the filters were incubated overnight in 3% BSA in TBS, then incubated 4 hr in 3% BSA containing 3 μg/ml anti-phosphotyrosine antibodies.

## 2. Cek8 expression and activity during development

In whole embryo extracts, Cek8 expression was detectable at embryonic day 3, increased gradually between embryonic days 3 and 5, then remained relatively constant through embryonic day 10, which was the last timepoint examined. Cek8 was phosphorylated on tyrosine *in vivo* at a low level in 10 day embryonic brain. In addition, Cek8 underwent autophosphorylation on tyrosine *in vitro* in the presence of ATP and divalent metal ions.

Cek8 expression also was examined in various tissues of 10 day chicken embryos. Cek8 was most abundant

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in the brain and retina, was expressed at substantial levels in thigh, gizzard and lungs and at lower levels in intestine, liver, lens and heart. Cek8 was not detectable in blood.

5           The developmental regulation of Cek8 expression was examined in greater detail in cerebrum, cerebellum, retina and thigh. In the cerebrum, Cek8 expression is low at embryonic day 6, then gradually increases to a maximal level at embryonic days 16 to 20. Cek8 expression is low,  
10 but detectable, in adult cerebrum. In contrast, expression in the cerebellum is low at embryonic day 12 and barely detectable at later stages of development. In thigh muscle, Cek8 expression is highest at embryonic day 7, then decreases to barely detectable levels by day 13, before  
15 terminal skeletal muscle differentiation occurs. In the retina, Cek8 expression remains relatively constant from embryonic day 8 until hatching.

Cek 8 expression also was examined by immunoperoxidase staining in chicken embryo frozen tissue  
20 sections. Embryos were removed from eggs, fixed in 4% formaldehyde, 0.1 mM sodium orthovanadate in PBS for 16 to 24 hr, then cryoprotected in 20% sucrose in PBS, 0.1 mM sodium orthovanadate for 24 hr. Embryos were embedded in OCT compound (Miles Inc.; Tarrytown NY), then frozen in dry  
25 ice/2-methylbutane. Ten  $\mu$ m cryostat sections were collected on glass slides and stored at -70 °C.

The sections were treated with 0.3% hydrogen peroxide for 10 min, then blocked with 3% BSA or normal goat or horse serum in PBS for 30 min. Sections were  
30 incubated with rabbit anti-Cek8 antibodies (10-20  $\mu$ g/ml) or mouse anti-200 kDa neurofilament protein antibodies (1  $\mu$ g/ml; Boehringer Mannheim; Indianapolis IN) in a 1:50 dilution of normal goat serum or horse serum for 30 min.

Controls were performed using anti-Cek8 antibodies that were preincubated with the antigen.

Following incubation with the primary antibody, the sections were rinsed with PBS and incubated with  
5 biotinylated goat anti-rabbit or horse anti-mouse IgG (Vector Labs; Burlingame CA). After additional washes with PBS, the sections were incubated with an avidin-biotin-  
peroxidase complex or with an avidin-biotin-alkaline  
10 phosphatase complex (Vector Labs). Following several washes in PBS, peroxidase or alkaline phosphatase were  
visualized using the appropriate substrate kit (Vector Labs). The sections then were rinsed in PBS, air dried,  
mounted in Permount and sealed with a #1 coverslip. Specimens were photographed with a Zeiss 405M inverted  
15 microscope.

Cek8 immunoreactivity was intense in the spinal cord and the spinal nerves. Localization of Cek8 in the  
spinal nerves was similar to that of a 200 kDa neurofilament protein. At embryonic day 6, Cek8 expression  
20 was restricted to the ventral portions of the spinal nerves, which contain axons of motor neurons.

The results of these experiments indicate that Cek8 is expressed early in development. In general, Cek8  
expression is lower early in embryogenesis than at later  
25 stages. Cek8 is differentially regulated in different tissues during development and expression is highest in the nervous system but also occurs in non-neuronal tissues. In  
view of these results, aberrant Cek8 expression or  
expression of an aberrant Cek8 protein can affect  
30 development by causing defective signal transduction throughout an organism.

### 3. Cek8 expression and activity in tumor cells

Protein tyrosine kinase activity is tightly regulated in normal tissues and, in the tissues described above, Cek8 was phosphorylated on tyrosine at a low level. It is well known that uncontrolled tyrosine kinase activity can lead to neoplastic transformation (Bishop, J.M., Cell 64:234-248 (1991)). Therefore, the expression and activation of Cek8 in a number of tumor cell lines was examined.

Because of the predominant expression of Cek8 in the brain and retina, Cek8 expression and activity was determined in a number of cell lines, B50, B49, B35, B28 and B23, which were derived from CNS system (CNS) tumors (Schubert et al., Nature 249:224-227 (1974), which is incorporated herein by reference). B35 and B50 cells have neuronal properties and both expressed Cek8. However, Cek8 is substantially phosphorylated on tyrosine only in B50 cells (Figures 5.A. and 5.B.). B28 and B49 cells, which display glial characteristics, both expressed a moderate level of Cek8 that is phosphorylated on tyrosine. B23 cells did not have detectable levels of Cek8.

The highest level of Cek8 expression was found in undifferentiated P19 embryonal carcinoma cells (McBurney and Rogers, J. Devel. Biol. 89:503-508 (1982), which is incorporated herein by reference) and in HaCaT keratinocytes (Boukamp et al., J. Cell Biol. 106:761-770 (1988), which is incorporated herein by reference). In both of these cell lines, Cek8 was phosphorylated on tyrosine. Furthermore, comparable levels of Cek8 expression were observed in normal and Rous sarcoma virus-transformed chicken embryo fibroblasts. However, Cek8 was substantially phosphorylated on tyrosine only in the transformed cells (Figures 6.C. and 6.D.). In addition, in

LMH cells, which were derived from a hepatocellular carcinoma (Kawaguchi et al., Canc. Res. 47:4460-4464 (1987), which is incorporated herein by reference), Cek8 is highly phosphorylated on tyrosine as compared to adult or embryonic liver (Figures 6.A. and 6.B.).

For comparison, Cek5 expression and activation also was examined in the CNS tumor-derived cell lines. Cek5 was immunoprecipitated using anti-Cek5 antibodies followed by immunoblotting with anti-phosphotyrosine antibodies. Cek 5 was expressed in all of the cell lines derived from tumors of the CNS, with the highest expression in the B35 cells and the B49 cells. Tyrosine phosphorylation of Cek5 was observed in B28, B49 and B50 cells (Figures 5.C. and 5.D.). Cek5 also was highly expressed and phosphorylated in P19 cells and HaCaT cells. Thus, Cek5 expression and activation is similar, but not identical, to Cek8 expression and activation in tumor cells.

#### 4. Effect of tyrosine phosphorylation on Cek8 kinase activity

The effect of tyrosine phosphorylation on the *in vitro* catalytic activity of Cek8 also was examined. *In vivo* substrates of Cek8 have not yet been identified. Therefore, a fusion protein consisting of the C-terminal 117 amino acids of Cek4 fused to  $\beta$ -galactosidase was used as an exogenous substrate. The fusion protein was purified from bacterial extracts by SDS-PAGE and eluted from the gel.

Assays were performed by incubating 1  $\mu$ g fusion protein substrate with Cek8 immunoprecipitate. Cek8 was immunoprecipitated from 10 day chick embryonic brain using 10  $\mu$ g anti-Cek8 antibodies and 5  $\mu$ l Staph A and was complexed to the antibodies and Staph A when the substrate was added. In some cases, Cek8 was phosphorylated for 1 hr

using the *in vitro* kinase reaction described above, in order to obtain Cek8 in a highly tyrosine-phosphorylated form. The fusion protein substrate then was added and phosphorylation of the substrate was allowed to proceed for 5 1 min at 0 °C or 37 °C in the phosphorylation buffer described above containing 200  $\mu$ M ATP. In parallel experiments, Cek8 that was not phosphorylated *in vitro* was used in the assay.

Following incubation, the samples were 10 centrifuged briefly in a microfuge, 100  $\mu$ l 1% SDS in PBS was added to the pellets and the samples were heated at 95 °C for 5 min. The samples were centrifuged for 3 min and the supernatants were transferred to tubes containing anti- $\beta$ -galactosidase antibodies bound to Staph A beads in 900  $\mu$ l 15 RIPA buffer lacking SDS. Immunoprecipitation was performed as described above and the extent of tyrosine phosphorylation of the immunoprecipitated fusion protein substrate was analyzed by immunoblotting using anti-phosphotyrosine antibodies.

20 As shown in Figure 6.E., the phosphorylated form of Cek8 produced a greater amount of phosphorylation of the substrate on tyrosine at both 0 °C or 37 °C. These results indicate that activation of Cek8 by tyrosine phosphorylation increases the kinase activity of Cek8.

25 Although the invention has been described with reference to the disclosed embodiments, it should be understood that various modifications can be made without departing from the spirit of the invention. Accordingly, the invention is limited only by the following claims.

## SEQUENCE LISTING

## (1) GENERAL INFORMATION:

- (i) APPLICANT: LA JOLLA CANCER RESEARCH FOUNDATION
- (ii) TITLE OF INVENTION: NOVEL EPH-RELATED TYROSINE KINASES,  
NUCLEOTIDE SEQUENCES, AND METHODS OF USE
- (iii) NUMBER OF SEQUENCES: 26
- (iv) CORRESPONDENCE ADDRESS:
  - (A) ADDRESSEE: CAMPBELL AND FLORES
  - (B) STREET: 4370 La Jolla Village Drive, Suite 700
  - (C) CITY: San Diego
  - (D) STATE: California
  - (E) COUNTRY: United States of America
  - (F) ZIP: 92122
- (v) COMPUTER READABLE FORM:
  - (A) MEDIUM TYPE: Floppy disk
  - (B) COMPUTER: IBM PC compatible
  - (C) OPERATING SYSTEM: PC-DOS/MS-DOS
  - (D) SOFTWARE: PatentIn Release #1.0, Version #1.25
- (vi) CURRENT APPLICATION DATA:
  - (A) APPLICATION NUMBER:
  - (B) FILING DATE: 07-Sep-1994
  - (C) CLASSIFICATION:
- (viii) ATTORNEY/AGENT INFORMATION:
  - (A) NAME: Imbra, Richard J.
  - (B) REGISTRATION NUMBER: 37,643
  - (C) REFERENCE/DOCKET NUMBER: FP-LJ 1114
- (ix) TELECOMMUNICATION INFORMATION:
  - (A) TELEPHONE: (619) 535-9001
  - (B) TELEFAX: (619) 535-8949

## (2) INFORMATION FOR SEQ ID NO:1:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 3133 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: both
  - (D) TOPOLOGY: linear
- (ix) FEATURE:
  - (A) NAME/KEY: CDS
  - (B) LOCATION: join(3..419, 421..2858)
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:
 

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	Glu	Thr	Leu	Met	Asp	Thr	Arg	Thr	Ala	Thr	Ala	Glu	Leu	Gly	Trp	
1					5					10					15	
ACT	GCC	AAC	CCT	CCG	TCA	GGG	TGG	GAA	GAA	GTG	AGT	GGC	TAC	GAC	GAG	95
Thr	Ala	Asn	Pro	Pro	Ser	Gly	Trp	Glu	Glu	Val	Ser	Gly	Tyr	Asp	Glu	
				20					25						30	

38

AAC	CTG	AAC	ACC	ATC	CGT	ACC	TAC	CAG	GTG	TGC	AAC	GTC	TTC	GAG	CCA	143
Asn	Leu	Asn	Thr	Ile	Arg	Thr	Tyr	Gln	Val	Cys	Asn	Val	Phe	Glu	Pro	
		35						40					45			
AAC	CAG	AAC	AAC	TGG	CTC	CTC	ACC	ACC	TTC	ATC	AAC	CGG	CGC	GGA	GCC	191
Asn	Gln	Asn	Asn	Trp	Leu	Leu	Thr	Thr	Phe	Ile	Asn	Arg	Arg	Gly	Ala	
		50					55					60				
CAC	CGC	ATC	TAC	ACT	GAG	ATG	CGC	TTC	ACT	GTG	CGG	GAC	TGC	AGC	AGC	239
His	Arg	Ile	Tyr	Thr	Glu	Met	Arg	Phe	Thr	Val	Arg	Asp	Cys	Ser	Ser	
	65					70					75					
CTC	CCC	AAC	GTC	CCC	GGC	TCC	TGC	AAG	GAG	ACC	TTC	AAC	CTC	TAC	TAC	287
Leu	Pro	Asn	Val	Pro	Gly	Ser	Cys	Lys	Glu	Thr	Phe	Asn	Leu	Tyr	Tyr	
80					85					90				95		
TAT	GAG	ACA	GAC	TCT	GTC	ATT	GCC	ACT	AAG	AAG	TCG	GCC	TTC	TGG	ACG	335
Tyr	Glu	Thr	Asp	Ser	Val	Ile	Ala	Thr	Lys	Lys	Ser	Ala	Phe	Trp	Thr	
				100					105					110		
GAG	GCA	CCC	TAC	CTC	AAA	GTG	GAC	ACC	ATT	GCT	GCT	GAC	GAG	AGC	TTT	383
Glu	Ala	Pro	Tyr	Leu	Lys	Val	Asp	Thr	Ile	Ala	Ala	Asp	Glu	Ser	Phe	
			115					120					125			
TCC	CAG	GTG	GAC	TTT	GGT	GGC	AGG	TTG	ATG	AAG	GGT	T	TTC	TTC	AAG	429
Ser	Gln	Val	Asp	Phe	Gly	Gly	Arg	Leu	Met	Lys	Gly		Phe	Phe	Lys	
		130					135						140			
AAG	TGC	CCA	AGC	GTG	GTG	CAG	AAC	TTC	GCT	ATC	TTC	CCT	GAG	ACG	ATG	477
Lys	Cys	Pro	Ser	Val	Val	Gln	Asn	Phe	Ala	Ile	Phe	Pro	Glu	Thr	Met	
		145					150					155				
ACG	GGG	GCA	GAG	AGC	ACC	TCT	CTG	GTG	ACA	GCA	CGG	GGC	ACC	TGC	ATC	525
Thr	Gly	Ala	Glu	Ser	Thr	Ser	Leu	Val	Thr	Ala	Arg	Gly	Thr	Cys	Ile	
	160					165					170					
CCC	AAC	GCT	GAG	GAG	GTG	GAC	GTG	CCC	ATC	AAG	CTG	TAC	TGC	AAC	GGG	573
Pro	Asn	Ala	Glu	Glu	Val	Asp	Val	Pro	Ile	Lys	Leu	Tyr	Cys	Asn	Gly	
175					180					185					190	
GAT	GGG	GAG	TGG	ATG	GTA	CCC	ATA	GGT	CGC	TGC	ACC	TGC	AAG	GCT	GGT	621
Asp	Gly	Glu	Trp	Met	Val	Pro	Ile	Gly	Arg	Cys	Thr	Cys	Lys	Ala	Gly	
				195					200					205		
TAT	GAG	CCG	GAA	AAC	AAC	GTG	GCT	TGC	AGA	GCC	TGC	CCG	GCT	GGG	ACA	669
Tyr	Glu	Pro	Glu	Asn	Asn	Val	Ala	Cys	Arg	Ala	Cys	Pro	Ala	Gly	Thr	
			210				215						220			
TTC	AAA	GCC	AGT	CAG	GGT	GCG	GGG	CTG	TGT	GCC	CGC	TGT	CCC	CCC	AAC	717
Phe	Lys	Ala	Ser	Gln	Gly	Ala	Gly	Leu	Cys	Ala	Arg	Cys	Pro	Pro	Asn	
	225						230					235				
AGC	CGC	TCC	AGC	GCC	GAG	GCC	TCA	CCG	CTC	TGC	GCC	TGC	CGC	AAC	GGC	765
Ser	Arg	Ser	Ser	Ala	Glu	Ala	Ser	Pro	Leu	Cys	Ala	Cys	Arg	Asn	Gly	
	240					245					250					
TAC	TTT	CGG	GCT	GAC	CTG	GAC	CCA	CCG	ACA	GCT	GCC	TGC	ACC	AGC	GTC	813
Tyr	Phe	Arg	Ala	Asp	Leu	Asp	Pro	Pro	Thr	Ala	Ala	Cys	Thr	Ser	Val	
255					260					265					270	
CCC	TCT	GGT	CCA	CGC	AAC	GTC	ATC	TCC	ATT	GTC	AAT	GAG	ACC	TCC	ATC	861
Pro	Ser	Gly	Pro	Arg	Asn	Val	Ile	Ser	Ile	Val	Asn	Glu	Thr	Ser	Ile	
				275					280					285		
ATC	CTG	GAG	TGG	AAC	CCG	CCA	CGG	GAG	ACA	GGA	GGC	CGG	GAT	GAT	GTC	909
Ile	Leu	Glu	Trp	Asn	Pro	Pro	Arg	Glu	Thr	Gly	Gly	Arg	Asp	Asp	Val	
			290					295					300			



ACT Thr	TAC Tyr	AAC Asn 305	ATT Ile	GTC Val	TGC Cys	AAG Lys 310	AAG Lys 310	TGC Cys	CGG Arg	GCA Ala	GAC Asp 315	CGG Arg 315	CGT Arg	GCC Ala	TGC Cys	957
TCC Ser	CGC Arg 320	TGC Cys	GAC Asp	GAC Asp	AAC Asn 325	GTG Val 325	GAG Glu	TTT Phe	GTG Val	CCC Pro 330	CGA Arg 330	CAG Gln	CTG Leu	GGG Gly	CTG Leu	1005
ACA Thr 335	GAG Glu	ACC Thr	CGC Arg	GTC Val	TTC Phe 340	ATC Ile	AGC Ser	AGC Ser	CTC Leu	TGG Trp 345	GCA Ala	CAC His	ACA Thr	CCC Pro 350	TAC Tyr 350	1053
ACC Thr	TTT Phe	GAG Glu	ATC Ile	CAG Gln 355	GCG Ala	GTC Val	AAC Asn	GGG Gly	GTT Val 360	TCC Ser	AAC Asn	AAG Lys	AGC Ser	CCC Pro 365	TTC Phe	1101
CCA Pro	CCC Pro	CAG Gln 370	CAC His 370	GTC Val	TCC Ser	GTG Val	AAC Asn 375	ATC Ile 375	ACC Thr	ACC Thr	AAC Asn	CAA Gln 380	GCT Ala 380	GCA Ala	CCC Pro	1149
TCC Ser	ACT Thr 385	GTC Val	CCC Pro	ATC Ile	ATG Met	CAC His	CAG Gln 390	GTG Val	AGT Ser	GCC Ala	ACC Thr	ATG Met 395	AGG Arg	AGC Ser	ATC Ile	1197
ACG Thr 400	CTA Leu	TCC Ser	TGG Trp	CCG Pro	CAG Gln 405	CCG Pro	GAG Glu 405	CAG Gln	CCC Pro	AAC Asn 410	GGC Gly 410	ATC Ile	ATC Ile	CTG Leu	GAC Asp	1245
TAC Tyr 415	GAG Glu	CTG Leu	CGC Arg	TAC Tyr 420	TAC Tyr	GAG Glu	AAG Lys	CTG Leu	AGC Ser	CGC Arg 425	ATC Ile	TGC Cys	ACG Thr	CCC Pro 430	GAT Asp 430	1293
GTC Val	AGC Ser	GGC Gly	ACT Thr 435	GTG Val 435	GGC Gly	TCG Ser	AGA Arg	CCG Pro 440	GCG Ala 440	GCG Ala	GAC Asp	CAC His	AAC Asn	GAG Glu 445	TAC Tyr 445	1341
AAC Asn	TCC Ser	TCT Ser 450	GTG Val 450	GCC Ala	CGC Arg	AGT Ser	CAG Gln 455	ACC Thr 455	AAC Asn	ACG Thr	GCC Ala	CGG Arg 460	CTG Leu 460	GAG Glu	GGG Gly	1389
CTG Leu	CGC Arg	CCT Pro 465	GGC Gly	ATG Met	GTG Val	TAC Tyr 470	GTG Val 470	GTG Val	CAG Gln	GTG Val	CGA Arg 475	GCA Ala 475	AGG Arg	ACG Thr	GTG Val	1437
GCC Ala 480	GGC Gly 480	TAT Tyr	GGG Gly	AAG Lys	TAC Tyr 485	AGT Ser 485	GGG Gly 485	AAG Lys	ATG Met	TGC Cys	TTC Phe 490	CAG Gln 490	ACA Thr	CTG Leu	ACC Thr	1485
GAT Asp 495	GAT Asp	GAC Asp	TAC Tyr	AAG Lys 500	TCT Ser 500	GAG Glu	CTG Leu	AGG Arg	GAG Glu	CAG Gln 505	CTG Leu	CCA Pro	TTG Leu	ATT Ile	GCG Ala 510	1533
GGG Gly	TCT Ser	GCA Ala	GCG Ala	GCC Ala 515	GGC Gly	GTG Val	GTC Val	TTC Phe 520	ATT Ile 520	GTT Val	TCG Ser	CTG Leu	GTG Val	GCC Ala 525	ATT Ile	1581
TCC Ser	ATA Ile	GTG Val 530	TGC Cys	AGC Ser	AGG Arg	AAG Lys	CGA Arg 535	GCG Ala 535	TAC Tyr	AGC Ser	AAG Lys	GAG Glu	GTC Val 540	GTT Val	TAC Tyr	1629
AGC Ser	GAT Asp 545	AAG Lys	CTG Leu	CAG Gln	CAC His	TAC Tyr 550	AGC Ser 550	ACC Thr	GGG Gly	AGA Arg	GGG Gly	TCT Ser 555	CCG Pro	GGA Gly	ATG Met	1677
AAG Lys 560	ATT Ile	TAC Tyr	ATC Ile	GAC Asp	CCC Pro	TTC Phe 565	ACT Thr 565	TAT Tyr	GAG Glu	GAC Asp	CCC Pro 570	AAC Asn	GAG Glu	GCA Ala	GTG Val	1725

CGT Arg 575	GAG Glu	TTC Phe	GCC Ala	AAG Lys	GAG Glu 580	ATT Ile	GAC Asp	GTC Val	TCC Ser	TTT Phe 585	GTG Val	AAG Lys	ATT Ile	GAA Glu	GAG Glu 590	1773
GTC Val	ATT Ile	GGA Gly	GCA Ala	GGG Gly 595	GAG Glu	TTT Phe	GGA Gly	GAG Glu	GTG Val 600	TAC Tyr	AAA Lys	GGC Gly	CGC Arg	CTG Leu	AAG Lys 605	1821
TTG Leu	CCT Pro	GGC Gly	AAG Lys 610	CGG Arg	GAG Glu	ATC Ile	TAT Tyr	GTG Val 615	GCC Ala	ATC Ile	AAA Lys	ACA Thr	CTG Leu 620	AAG Lys	GCT Ala	1869
GGC Gly	TAC Tyr	TCA Ser 625	GAG Glu	AAG Lys	CAG Gln	CGC Arg	CGG Arg 630	GAT Asp	TTC Phe	CTG Leu	AGC Ser	GAA Glu 635	GCC Ala	AGC Ser	ATC Ile	1917
ATG Met 640	GGG Gly	CAG Gln	TTT Phe	GAC Asp	CAC His	CCC Pro 645	AAC Asn	ATC Ile	ATC Ile	CGG Arg 650	CTG Leu	GAA Glu	GGG Gly	GTG Val	GTG Val	1965
ACC Thr 655	AAG Lys	AGC Ser	CGA Arg	CCA Pro	GTC Val 660	ATG Met	ATT Ile	ATC Ile	ACA Thr	GAG Glu 665	TTC Phe	ATG Met	GAG Glu	AAT Asn	GGG Gly 670	2013
GCC Ala	CTG Leu	GAC Asp	TCG Ser	TTC Phe 675	CTG Leu	CGG Arg	CAA Gln	AAT Asn	GAT Asp 680	GGG Gly	CAG Gln	TTC Phe	ACA Thr	GTG Val 685	ATC Ile	2061
CAG Gln	CTG Leu	GTG Val	GGG Gly 690	ATG Met	CTC Leu	AGA Arg	GGG Gly 695	ATT Ile	GCT Ala	GCT Ala	GGG Gly	ATG Met	AAG Lys 700	TAC Tyr	CTG Leu	2109
GCA Ala	GAG Glu	ATG Met 705	AAC Asn	TAT Tyr	GTC Val	CAC His	AGG Arg 710	GAT Asp	CTG Leu	GCG Ala	GCC Ala	AGG Arg 715	AAC Asn	ATT Ile	CTG Leu	2157
GTC Val	AAC Asn 720	AGC Ser	AAC Asn	CTG Leu	GTG Val	TGC Cys 725	AAA Lys	GTG Val	TCA Ser	GAC Asp	TTT Phe 730	GGC Gly	CTC Leu	TCG Ser	CGC Arg	2205
TAC Tyr 735	CTG Leu	CAG Gln	GAC Asp	GAC Asp	ACC Thr 740	TCT Ser	GAT Asp	CCC Pro	ACC Thr	TAC Tyr 745	ACC Thr	AGC Ser	TCC Ser	TTG Leu	GGT Gly 750	2253
GGG Gly	AAG Lys	ATC Ile	CCT Pro	GTG Val 755	CGA Arg	TGG Trp	ACA Thr	GCA Ala	CCA Pro 760	GAG Glu	GCC Ala	ATT Ile	GCG Ala	TAC Tyr 765	CGC Arg	2301
AAG Lys	TTC Phe	ACG Thr	TCA Ser 770	GCC Ala	AGT Ser	GAC Asp	GTC Val 775	TGG Trp	AGC Ser	TAT Tyr	GGC Gly	ATC Ile	GTC Val 780	ATG Met	TGG Trp	2349
GAG Glu	GTG Val	ATG Met 785	TCG Ser	TTC Phe	GGA Gly	GAG Glu	AGG Arg 790	CCC Pro	TAC Tyr	TGG Trp	GAC Asp	ATG Met 795	TCC Ser	AAC Asn	CAG Gln	2397
GAC Asp 800	GTC Val	ATC Ile	AAT Asn	GCC Ala	ATC Ile	GAG Glu 805	CAG Gln	GAC Asp	TAC Tyr	CGG Arg	CTC Leu 810	CCG Pro	CCG Pro	CCC Pro	ATG Met	2445
GAC Asp 815	TGC Cys	CCA Pro	GCT Ala	GCC Ala	CTG Leu 820	CAC His	CAA Gln	CTG Leu	ATG Met	CTG Leu 825	GAC Asp	TGC Cys	TGG Trp	CAG Gln	AAG Lys 830	2493
GAC Asp	CGC Arg	AAC Asn	ACC Thr	CGG Arg 835	CCT Pro	CGC Arg	TTG Leu	GCC Ala	GAG Glu 840	ATT Ile	GTC Val	AAC Asn	ACC Thr	CTG Leu 845	GAC Asp	2541

41

AAA ATG ATC CGC AAC CCG GCA AGC CTC AAA ACT GTG GCT ACC ATC ACC	2589
Lys Met Ile Arg Asn Pro Ala Ser Leu Lys Thr Val Ala Thr Ile Thr	
850 855 860	
GCT GTG CCT TCT CAG CCC CTC CTC GAC CGC TCT ATC CCT GAT TTC ACT	2637
Ala Val Pro Ser Gln Pro Leu Leu Asp Arg Ser Ile Pro Asp Phe Thr	
865 870 875	
GCC TTT ACC TCA GTA GAA GAC TGG CTG AGT GCC GTC AAG ATG AGC CAG	2685
Ala Phe Thr Ser Val Glu Asp Trp Leu Ser Ala Val Lys Met Ser Gln	
880 885 890	
TAT AGA GAC AAC TTC CTG AGC GCT GGA TTC ACC TCC CTC CAG CTG GTC	2733
Tyr Arg Asp Asn Phe Leu Ser Ala Gly Phe Thr Ser Leu Gln Leu Val	
895 900 905 910	
GCC CAG ATG ACA TCT GAA GAC CTC CTG AGA ATA GGA GTA ACG CTG GCT	2781
Ala Gln Met Thr Ser Glu Asp Leu Leu Arg Ile Gly Val Thr Leu Ala	
915 920 925	
GGG CAC CAG AAG AAG ATC CTG AAC AGC ATC CAG TCC ATG CGC GTG CAG	2829
Gly His Gln Lys Lys Ile Leu Asn Ser Ile Gln Ser Met Arg Val Gln	
930 935 940	
ATG AGT CAG TCT CCG ACC TCG ATG GCGTGACGTC CCTCGCTCGA CGAGGAGGGG	2883
Met Ser Gln Ser Pro Thr Ser Met Ala	
945 950	
GACGGGGAGG GCAGGTGGCA GAGGTGGGAG GGGAGGAACT GATCTGATGG GAGCCGTGGG	2943
GCCGCAGCTG GAGAGGGGCA GCCACGGCCG GGGCTGTGCC TGACCGCGGA GGACGTTCTT	3003
GGGACTCGCC TCGGCCTGGT GACTTCCATC CCTCACCAAC AGAAGCACAC TTACCGATGT	3063
CACGGGGGAC AGCGTATAAA TAAGTATAAA TATGTACAAA TCATATATTT AAAAAAAAAA	3123
AAAAAAAAAAG	3133

## (2) INFORMATION FOR SEQ ID NO:2:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 951 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: protein

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Glu Thr Leu Met Asp Thr Arg Thr Ala Thr Ala Glu Leu Gly Trp Thr	
1 5 10 15	
Ala Asn Pro Pro Ser Gly Trp Glu Glu Val Ser Gly Tyr Asp Glu Asn	
20 25 30	
Leu Asn Thr Ile Arg Thr Tyr Gln Val Cys Asn Val Phe Glu Pro Asn	
35 40 45	
Gln Asn Asn Trp Leu Leu Thr Thr Phe Ile Asn Arg Arg Gly Ala His	
50 55 60	
Arg Ile Tyr Thr Glu Met Arg Phe Thr Val Arg Asp Cys Ser Ser Leu	
65 70 75 80	
Pro Asn Val Pro Gly Ser Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Tyr	
85 90 95	

Glu Thr Asp Ser Val Ile Ala Thr Lys Lys Ser Ala Phe Trp Thr Glu  
                   100                                  105                                  110  
 Ala Pro Tyr Leu Lys Val Asp Thr Ile Ala Ala Asp Glu Ser Phe Ser  
                   115                                  120                                  125  
 Gln Val Asp Phe Gly Gly Arg Leu Met Lys Gly Phe Phe Lys Lys Cys  
                   130                                  135                                  140  
 Pro Ser Val Val Gln Asn Phe Ala Ile Phe Pro Glu Thr Met Thr Gly  
                   145                                  150                                  155                                  160  
 Ala Glu Ser Thr Ser Leu Val Thr Ala Arg Gly Thr Cys Ile Pro Asn  
                                   165                                  170                                  175  
 Ala Glu Glu Val Asp Val Pro Ile Lys Leu Tyr Cys Asn Gly Asp Gly  
                                   180                                  185                                  190  
 Glu Trp Met Val Pro Ile Gly Arg Cys Thr Cys Lys Ala Gly Tyr Glu  
                   195                                  200                                  205  
 Pro Glu Asn Asn Val Ala Cys Arg Ala Cys Pro Ala Gly Thr Phe Lys  
                   210                                  215                                  220  
 Ala Ser Gln Gly Ala Gly Leu Cys Ala Arg Cys Pro Pro Asn Ser Arg  
                   225                                  230                                  235                                  240  
 Ser Ser Ala Glu Ala Ser Pro Leu Cys Ala Cys Arg Asn Gly Tyr Phe  
                                   245                                  250                                  255  
 Arg Ala Asp Leu Asp Pro Pro Thr Ala Ala Cys Thr Ser Val Pro Ser  
                   260                                  265                                  270  
 Gly Pro Arg Asn Val Ile Ser Ile Val Asn Glu Thr Ser Ile Ile Leu  
                   275                                  280                                  285  
 Glu Trp Asn Pro Pro Arg Glu Thr Gly Gly Arg Asp Asp Val Thr Tyr  
                   290                                  295                                  300  
 Asn Ile Val Cys Lys Lys Cys Arg Ala Asp Arg Arg Ala Cys Ser Arg  
                   305                                  310                                  315                                  320  
 Cys Asp Asp Asn Val Glu Phe Val Pro Arg Gln Leu Gly Leu Thr Glu  
                                   325                                  330                                  335  
 Thr Arg Val Phe Ile Ser Ser Leu Trp Ala His Thr Pro Tyr Thr Phe  
                                   340                                  345                                  350  
 Glu Ile Gln Ala Val Asn Gly Val Ser Asn Lys Ser Pro Phe Pro Pro  
                   355                                  360                                  365  
 Gln His Val Ser Val Asn Ile Thr Thr Asn Gln Ala Ala Pro Ser Thr  
                   370                                  375                                  380  
 Val Pro Ile Met His Gln Val Ser Ala Thr Met Arg Ser Ile Thr Leu  
                   385                                  390                                  395                                  400  
 Ser Trp Pro Gln Pro Glu Gln Pro Asn Gly Ile Ile Leu Asp Tyr Glu  
                                   405                                  410                                  415  
 Leu Arg Tyr Tyr Glu Lys Leu Ser Arg Ile Cys Thr Pro Asp Val Ser  
                                   420                                  425                                  430  
 Gly Thr Val Gly Ser Arg Pro Ala Ala Asp His Asn Glu Tyr Asn Ser  
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Ser	Val	Ala	Arg	Ser	Gln	Thr	Asn	Thr	Ala	Arg	Leu	Glu	Gly	Leu	Arg
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Pro	Gly	Met	Val	Tyr	Val	Val	Gln	Val	Arg	Ala	Arg	Thr	Val	Ala	Gly
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Tyr	Gly	Lys	Tyr	Ser	Gly	Lys	Met	Cys	Phe	Gln	Thr	Leu	Thr	Asp	Asp
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Ala	Ala	Ala	Gly	Val	Val	Phe	Ile	Val	Ser	Leu	Val	Ala	Ile	Ser	Ile
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	530					535					540				
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Tyr	Ile	Asp	Pro	Phe	Thr	Tyr	Glu	Asp	Pro	Asn	Glu	Ala	Val	Arg	Glu
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Phe	Ala	Lys	Glu	Ile	Asp	Val	Ser	Phe	Val	Lys	Ile	Glu	Glu	Val	Ile
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Gly	Ala	Gly	Glu	Phe	Gly	Glu	Val	Tyr	Lys	Gly	Arg	Leu	Lys	Leu	Pro
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Gly	Lys	Arg	Glu	Ile	Tyr	Val	Ala	Ile	Lys	Thr	Leu	Lys	Ala	Gly	Tyr
	610					615					620				
Ser	Glu	Lys	Gln	Arg	Arg	Asp	Phe	Leu	Ser	Glu	Ala	Ser	Ile	Met	Gly
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Gln	Phe	Asp	His	Pro	Asn	Ile	Ile	Arg	Leu	Glu	Gly	Val	Val	Thr	Lys
				645					650					655	
Ser	Arg	Pro	Val	Met	Ile	Ile	Thr	Glu	Phe	Met	Glu	Asn	Gly	Ala	Leu
			660					665					670		
Asp	Ser	Phe	Leu	Arg	Gln	Asn	Asp	Gly	Gln	Phe	Thr	Val	Ile	Gln	Leu
		675					680					685			
Val	Gly	Met	Leu	Arg	Gly	Ile	Ala	Ala	Gly	Met	Lys	Tyr	Leu	Ala	Glu
	690					695					700				
Met	Asn	Tyr	Val	His	Arg	Asp	Leu	Ala	Ala	Arg	Asn	Ile	Leu	Val	Asn
705					710					715					720
Ser	Asn	Leu	Val	Cys	Lys	Val	Ser	Asp	Phe	Gly	Leu	Ser	Arg	Tyr	Leu
				725					730					735	
Gln	Asp	Asp	Thr	Ser	Asp	Pro	Thr	Tyr	Thr	Ser	Ser	Leu	Gly	Gly	Lys
			740					745					750		
Ile	Pro	Val	Arg	Trp	Thr	Ala	Pro	Glu	Ala	Ile	Ala	Tyr	Arg	Lys	Phe
		755					760					765			
Thr	Ser	Ala	Ser	Asp	Val	Trp	Ser	Tyr	Gly	Ile	Val	Met	Trp	Glu	Val
						775					780				
Met	Ser	Phe	Gly	Glu	Arg	Pro	Tyr	Trp	Asp	Met	Ser	Asn	Gln	Asp	Val
785					790					795					800



45

GGA	TTT	TAC	CTT	GCT	TTC	CAG	GAT	GTG	GGC	GCC	TGC	ATT	GCC	CTG	GTC	286
Gly	Phe	Tyr	Leu	Ala	Phe	Gln	Asp	Val	Gly	Ala	Cys	Ile	Ala	Leu	Val	
80					85				90						95	
TCT	GTG	CGT	GTG	TAC	TAC	AAG	AAA	TGC	CCA	TCA	GTG	ATC	CGC	AAC	CTG	334
Ser	Val	Arg	Val	Tyr	Tyr	Lys	Lys	Cys	Pro	Ser	Val	Ile	Arg	Asn	Leu	
				100					105					110		
GCA	CGC	TTT	CCA	GAT	ACC	ATC	ACA	GGA	GCA	GAT	TCC	TCG	CAG	CTG	CTA	382
Ala	Arg	Phe	Pro	Asp	Thr	Ile	Thr	Gly	Ala	Asp	Ser	Ser	Gln	Leu	Leu	
			115					120					125			
GAA	GTG	TCA	GGC	GTC	TGT	GTC	AAC	CAC	TCA	GTG	ACT	GAT	GAG	GCA	CCA	430
Glu	Val	Ser	Gly	Val	Cys	Val	Asn	His	Ser	Val	Thr	Asp	Glu	Ala	Pro	
		130					135					140				
AAG	ATG	CAC	TGC	AGT	TCA	GAG	GGA	GAA	TGG	CTG	GTG	CCC	ATT	GGG	AAG	478
Lys	Met	His	Cys	Ser	Ser	Glu	Gly	Glu	Trp	Leu	Val	Pro	Ile	Gly	Lys	
	145					150					155					
TGT	TTG	TGC	AAG	GCA	GGG	TAC	GAG	GAG	AAG	AAC	AAC	ACC	TGC	CAA	GCA	526
Cys	Leu	Cys	Lys	Ala	Gly	Tyr	Glu	Glu	Lys	Asn	Asn	Thr	Cys	Gln	Ala	
160					165					170					175	
CCT	TCT	CCA	GTC	AGT	AGT	GTG	AAA	AAA	GGG	AAG	ATA	ACT	AAA	AAT	AGC	574
Pro	Ser	Pro	Val	Ser	Ser	Val	Lys	Lys	Gly	Lys	Ile	Thr	Lys	Asn	Ser	
				180					185					190		
ATC	TCC	CTT	TCC	TGG	CAG	GAG	CCA	GAT	CGA	CCC	AAC	GGC	ATC	ATC	CTG	622
Ile	Ser	Leu	Ser	Trp	Gln	Glu	Pro	Asp	Arg	Pro	Asn	Gly	Ile	Ile	Leu	
			195					200					205			
GAA	TAC	GAA	ATC	AAA	TAT	TTT	GAA	AAG	GAC	CAG	GAG	ACA	AGC	TAC	ACC	670
Glu	Tyr	Glu	Ile	Lys	Tyr	Phe	Glu	Lys	Asp	Gln	Glu	Thr	Ser	Tyr	Thr	
		210					215					220				
ATC	ATC	AAA	TCC	AAA	GAG	ACC	GCA	ATT	ACG	GCA	GAT	GGC	TTG	AAA	CCA	718
Ile	Ile	Lys	Ser	Lys	Glu	Thr	Ala	Ile	Thr	Ala	Asp	Gly	Leu	Lys	Pro	
		225				230					235					
GGC	TCA	GCG	TAC	GTC	TTC	CAG	ATC	CGA	GCC	CGG	ACA	GCT	GCT	GGC	TAC	766
Gly	Ser	Ala	Tyr	Val	Phe	Gln	Ile	Arg	Ala	Arg	Thr	Ala	Ala	Gly	Tyr	
240					245					250					255	
GGT	GGC	TTC	AGT	CGA	AGA	TTT	GAG	TTT	GAA	ACC	AGC	CCA	GTG	TTA	GCT	814
Gly	Gly	Phe	Ser	Arg	Arg	Phe	Glu	Phe	Glu	Thr	Ser	Pro	Val	Leu	Ala	
				260					265					270		
GCA	TCC	AGT	GAC	CAG	AGC	CAG	ATT	CCT	ATA	ATT	GTT	GTG	TCT	GTA	ACA	862
Ala	Ser	Ser	Asp	Gln	Ser	Gln	Ile	Pro	Ile	Ile	Val	Val	Ser	Val	Thr	
			275					280					285			
GTG	GGA	GTT	ATT	CTG	CTG	GCT	GTT	GTT	ATC	GGT	TTC	CTT	CTC	AGT	GGA	910
Val	Gly	Val	Ile	Leu	Leu	Ala	Val	Val	Ile	Gly	Phe	Leu	Leu	Ser	Gly	
		290					295					300				
AGG	CGC	TGT	GGC	TAC	AGC	AAG	GCT	AAA	CAA	GAC	CCA	GAA	GAA	GAA	AAG	958
Arg	Arg	Cys	Gly	Tyr	Ser	Lys	Ala	Lys	Gln	Asp	Pro	Glu	Glu	Glu	Lys	
		305				310					315					
ATG	CAT	TTT	CAT	AAT	GGC	CAC	ATT	AAA	CTG	CCT	GGT	GTA	AGA	ACC	TAC	1006
Met	His	Phe	His	Asn	Gly	His	Ile	Lys	Leu	Pro	Gly	Val	Arg	Thr	Tyr	
320					325					330					335	
ATT	GAT	CCC	CAC	ACC	TAT	GAG	GAC	CCT	AAT	CAA	GCT	GTC	CAC	GAG	TTT	1054
Ile	Asp	Pro	His	Thr	Tyr	Glu	Asp	Pro	Asn	Gln	Ala	Val	His	Glu	Phe	
				340					345					350		

GCC Ala	AAG Lys	GAA Glu	ATA Ile	GAA Glu	GCT Ala	TCG Ser	TGC Cys	ATA Ile	ACC Thr	ATC Ile	GAG Glu	AGA Arg	GTT Val	ATC Ile	GGA Gly	1102
			355				360						365			
GCT Ala	GGT Gly	GAA Glu	TTT Phe	GGA Gly	GAA Glu	GTC Val	TGC Cys	AGT Ser	GGA Gly	CGG Arg	CTG Leu	AAA Lys	CTG Leu	CAG Gln	GGA Gly	1150
			370				375					380				
AAA Lys	CGC Arg	GAG Glu	TTT Phe	CCA Pro	GTG Val	GCT Ala	ATC Ile	AAA Lys	ACC Thr	CTG Leu	AAG Lys	GTG Val	GGC Gly	TAC Tyr	ACA Thr	1198
			385				390					395				
GAG Glu	AAG Lys	CAA Gln	AGG Arg	CGA Arg	GAT Asp	TTC Phe	CTG Leu	GGA Gly	GAA Glu	GCG Ala	AGC Ser	ATC Ile	ATG Met	GGG Gly	CAG Gln	1246
			400				405				410					415
TTC Phe	GAC Asp	CAC His	CCC Pro	AAC Asn	ATC Ile	ATC Ile	CAC His	CTG Leu	GAA Glu	GGT Gly	GTC Val	GTC Val	ACA Thr	AAA Lys	AGC Ser	1294
				420						425					430	
AAA Lys	CCT Pro	GTA Val	ATG Met	ATA Ile	GTA Val	ACG Thr	GAA Glu	TAC Tyr	ATG Met	GAA Glu	AAT Asn	GGT Gly	TCT Ser	CTG Leu	GAT Asp	1342
			435					440					445			
ACA Thr	TTT Phe	TTA Leu	AAG Lys	AAG Lys	AAC Asn	GAT Asp	GGG Gly	CAG Gln	TTC Phe	ACG Thr	GTC Val	ATT Ile	CAG Gln	CTG Leu	GTC Val	1390
			450				455						460			
GGG Gly	ATG Met	CTG Leu	CGA Arg	GGC Gly	ATC Ile	GCA Ala	TCA Ser	GGG Gly	ATG Met	AAG Lys	TAC Tyr	CTG Leu	TCT Ser	GAC Asp	ATG Met	1438
			465				470					475				
GGT Gly	TAC Tyr	GTA Val	CAC His	AGA Arg	GAC Asp	CTC Leu	GCT Ala	GCC Ala	AGG Arg	AAT Asn	ATC Ile	CTC Leu	ATC Ile	AAC Asn	AGC Ser	1486
			480				485			490					495	
AAC Asn	TTA Leu	GTC Val	TGC Cys	AAG Lys	GTG Val	TCT Ser	GAC Asp	TTT Phe	GGC Gly	CTC Leu	TCC Ser	AGA Arg	GTC Val	CTA Leu	GAA Glu	1534
				500						505				510		
GAT Asp	GAT Asp	CCT Pro	GAA Glu	GCA Ala	GCG Ala	TAC Tyr	ACA Thr	ACC Thr	AGG Arg	GGA Gly	GGG Gly	AAG Lys	ATC Ile	CCC Pro	ATC Ile	1582
			515					520					525			
CGA Arg	TGG Trp	ACG Thr	GCA Ala	CCT Pro	GAA Glu	GCA Ala	ATC Ile	GCC Ala	TTC Phe	CGC Arg	AAA Lys	TTC Phe	ACG Thr	TCG Ser	GCC Ala	1630
			530				535						540			
AGC Ser	GAT Asp	GTG Val	TGG Trp	AGC Ser	TAC Tyr	GGC Gly	ATT Ile	GTG Val	ATG Met	TGG Trp	GAA Glu	GTG Val	ATG Met	TCC Ser	TAT Tyr	1678
			545				550				555					
GGC Gly	GAG Glu	AGA Arg	CCT Pro	TAC Tyr	TGG Trp	GAA Glu	ATG Met	ACA Thr	AAC Asn	CAA Gln	GAT Asp	GTG Val	ATT Ile	AAA Lys	GCC Ala	1726
			560				565				570				575	
GTG Val	GAG Glu	GAA Glu	GGC Gly	TAT Tyr	CGC Arg	CTG Leu	CCA Pro	AGT Ser	CCC Pro	ATG Met	GAC Asp	TGC Cys	CCT Pro	GCT Ala	GCT Ala	1774
				580					585					590		
CTC Leu	TAC Tyr	CAG Gln	TTG Leu	ATG Met	CTT Leu	GAC Asp	TGC Cys	TGG Trp	CAG Gln	AAA Lys	GAC Asp	CGC Arg	AAC Asn	AGC Ser	AGG Arg	1822
			595					600					605			
CCC Pro	AAG Lys	TTT Phe	GAT Asp	GAA Glu	ATT Ile	GTC Val	AGC Ser	ATG Met	TTG Leu	GAC Asp	AAG Lys	CTC Leu	ATC Ile	CGT Arg	AAC Asn	1870
			610				615						620			



CCA AGC AGC TTG AAG ACG TTG GTT AAT GCA TCG AGC AGA GTA TCA AAT Pro Ser Ser Leu Lys Thr Leu Val Asn Ala Ser Ser Arg Val Ser Asn 625 630 635	1918
TTG TTG GTA GAA CAC AGT CCA GTG GGG AGC GGT GCC TAC AGG TCA GTG Leu Leu Val Glu His Ser Pro Val Gly Ser Gly Ala Tyr Arg Ser Val 640 645 650 655	1966
GGT GAG TGG CTG GAA GCC ATC AAA ATG GGT CGA TAC ACC GAG ATT TTC Gly Glu Trp Leu Glu Ala Ile Lys Met Gly Arg Tyr Thr Glu Ile Phe 660 665 670	2014
ATG GAG AAT GGA TAC AGT TCG ATG GAT TCT GTG GCT CAG GTG ACC CTA Met Glu Asn Gly Tyr Ser Ser Met Asp Ser Val Ala Gln Val Thr Leu 675 680 685	2062
GAG GAT TTG AGG CGG CTG GGA GTG ACA CTT GTT GGT CAC CAG AAG AAG Glu Asp Leu Arg Arg Leu Gly Val Thr Leu Val Gly His Gln Lys Lys 690 695 700	2110
ATA ATG AAC AGC CTT CAA GAG ATG AAG GTC CAG TTG GTG AAT GGG ATG Ile Met Asn Ser Leu Gln Glu Met Lys Val Gln Leu Val Asn Gly Met 705 710 715	2158
GTG CCA TTG TAACTCGGTT TTTAAGTCAC TTCCTCGAGT GGTCGGTCCT Val Pro Leu 720	2207
GCACCTTTGTA TACTAGCTCT GAGATTTATT TTGACTAAAG AAGAAAAAAG GGAAATTCAG	2267
TGGTTTCTGT AACTGAAGGA CGCTGGCTTC TGCCACAGCA TTTATAAAGC AGTGTTTGAC	2327
TGAAGTTTTC ATTTTCTTCC TATTTGTGTC CTCATTCTCA TGAAGTAAAT GTAACATGCA	2387
TGGAACATGG AAATGGATCT ACTGTACATG AGGTTACCCA ATTTCTTGCG CTTCAGCATG	2447
ACAACAGCAA GCCTTCCCAC CACATGTTGT CTATACATGG GAGATATATA TATATGCATA	2507
TATATATATA GCACCTTTAT ATACTGAATT ACAGCAGCAG CACATGTTAA TACTTCCAAG	2567
GACTTACTTG ACTAGAGAAG TTTTGCAGCC ATTGTGGGCT CACACAAGCT GCGGTTTACT	2627
GAAGTTTACT TCAAGTCTTA CTTGTCTACA GAAGTGTTATT GAAGAGCAAT ATGATTAGAT	2687
TATTTCTGGA TAGATATTTT GTTTTGTAAA TTTAAAAAAT CGTGTTACAC AGCGTTAAGT	2747
TATAGAGACT AGTGATATAA CATGTTGCTT GCTCAATGGC AAATACAATA CAGGGTGTAT	2807
ATTTTTTTCT CTCTGTGTG CAAAGTTCTT TTAGTTTGCT CTTCTGTGAG GATAATACGT	2867
TATGATGTAT ATACTGTACA GTTTGCTACA CATCAGGTAC AAGATTGGGG CTTTCTCAAT	2927
GTTTTGTTCT TTTTCCCTCT TTTGTTTCAT TTTGTCTTCC TTTTGTGTTA ACCACTATGC	2987
TTTGATTTTT TGCTGCTGTT TGGTTTGAGG CAACATATAA AGCTTTCAGG TGTTTTGATT	3047
ATAAAAAAAAA AG	3059

## (2) INFORMATION FOR SEQ ID NO:4:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 722 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: protein

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

```

Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Leu Pro Gly Gly Leu Gly
 1           5           10           15
Thr Cys Lys Glu Thr Phe Asn Met Tyr Tyr Phe Glu Ser Asp Asp Glu
          20          25          30
Asp Gly Arg Asn Ile Arg Glu Asn Gln Tyr Ile Lys Ile Asp Thr Ile
          35          40          45
Ala Ala Asp Glu Ser Phe Thr Glu Leu Asp Leu Gly Asp Arg Val Met
          50          55          60
Lys Leu Asn Thr Glu Val Arg Asp Val Gly Pro Leu Thr Lys Lys Gly
          65          70          75          80
Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Ile Ala Leu Val Ser
          85          90          95
Val Arg Val Tyr Tyr Lys Lys Cys Pro Ser Val Ile Arg Asn Leu Ala
          100          105          110
Arg Phe Pro Asp Thr Ile Thr Gly Ala Asp Ser Ser Gln Leu Leu Glu
          115          120          125
Val Ser Gly Val Cys Val Asn His Ser Val Thr Asp Glu Ala Pro Lys
          130          135          140
Met His Cys Ser Ser Glu Gly Glu Trp Leu Val Pro Ile Gly Lys Cys
          145          150          155          160
Leu Cys Lys Ala Gly Tyr Glu Glu Lys Asn Asn Thr Cys Gln Ala Pro
          165          170          175
Ser Pro Val Ser Ser Val Lys Lys Gly Lys Ile Thr Lys Asn Ser Ile
          180          185          190
Ser Leu Ser Trp Gln Glu Pro Asp Arg Pro Asn Gly Ile Ile Leu Glu
          195          200          205
Tyr Glu Ile Lys Tyr Phe Glu Lys Asp Gln Glu Thr Ser Tyr Thr Ile
          210          215          220
Ile Lys Ser Lys Glu Thr Ala Ile Thr Ala Asp Gly Leu Lys Pro Gly
          225          230          235          240
Ser Ala Tyr Val Phe Gln Ile Arg Ala Arg Thr Ala Ala Gly Tyr Gly
          245          250          255
Gly Phe Ser Arg Arg Phe Glu Phe Glu Thr Ser Pro Val Leu Ala Ala
          260          265          270
Ser Ser Asp Gln Ser Gln Ile Pro Ile Ile Val Val Ser Val Thr Val
          275          280          285
Gly Val Ile Leu Leu Ala Val Val Ile Gly Phe Leu Leu Ser Gly Arg
          290          295          300

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Arg Cys Gly Tyr Ser Lys Ala Lys Gln Asp Pro Glu Glu Glu Lys Met  
 305 310 315 320  
 His Phe His Asn Gly His Ile Lys Leu Pro Gly Val Arg Thr Tyr Ile  
 325 330 335  
 Asp Pro His Thr Tyr Glu Asp Pro Asn Gln Ala Val His Glu Phe Ala  
 340 345 350  
 Lys Glu Ile Glu Ala Ser Cys Ile Thr Ile Glu Arg Val Ile Gly Ala  
 355 360 365  
 Gly Glu Phe Gly Glu Val Cys Ser Gly Arg Leu Lys Leu Gln Gly Lys  
 370 375 380  
 Arg Glu Phe Pro Val Ala Ile Lys Thr Leu Lys Val Gly Tyr Thr Glu  
 385 390 395 400  
 Lys Gln Arg Arg Asp Phe Leu Gly Glu Ala Ser Ile Met Gly Gln Phe  
 405 410 415  
 Asp His Pro Asn Ile Ile His Leu Glu Gly Val Val Thr Lys Ser Lys  
 420 425 430  
 Pro Val Met Ile Val Thr Glu Tyr Met Glu Asn Gly Ser Leu Asp Thr  
 435 440 445  
 Phe Leu Lys Lys Asn Asp Gly Gln Phe Thr Val Ile Gln Leu Val Gly  
 450 455 460  
 Met Leu Arg Gly Ile Ala Ser Gly Met Lys Tyr Leu Ser Asp Met Gly  
 465 470 475 480  
 Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Ile Asn Ser Asn  
 485 490 495  
 Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Val Leu Glu Asp  
 500 505 510  
 Asp Pro Glu Ala Ala Tyr Thr Thr Arg Gly Gly Lys Ile Pro Ile Arg  
 515 520 525  
 Trp Thr Ala Pro Glu Ala Ile Ala Phe Arg Lys Phe Thr Ser Ala Ser  
 530 535 540  
 Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met Ser Tyr Gly  
 545 550 555 560  
 Glu Arg Pro Tyr Trp Glu Met Thr Asn Gln Asp Val Ile Lys Ala Val  
 565 570 575  
 Glu Glu Gly Tyr Arg Leu Pro Ser Pro Met Asp Cys Pro Ala Ala Leu  
 580 585 590  
 Tyr Gln Leu Met Leu Asp Cys Trp Gln Lys Asp Arg Asn Ser Arg Pro  
 595 600 605  
 Lys Phe Asp Glu Ile Val Ser Met Leu Asp Lys Leu Ile Arg Asn Pro  
 610 615 620  
 Ser Ser Leu Lys Thr Leu Val Asn Ala Ser Ser Arg Val Ser Asn Leu  
 625 630 635 640  
 Leu Val Glu His Ser Pro Val Gly Ser Gly Ala Tyr Arg Ser Val Gly  
 645 650 655

50

[illegible]

(2) INFORMATION FOR SEO ID NO:5:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 2820 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: both  
(D) TOPOLOGY: linear

(ix) **FEATURE:**

- (A) NAME/KEY: CDS  
(B) LOCATION: 2..2548

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

C	GGA	GAG	AGC	CAG	TTT	GCC	AAG	ATT	GAC	ACC	ATT	GCT	GCT	GAT	GAG	46
	Gly	Glu	Ser	Gln	Phe	Ala	Lys	Ile	Asp	Thr	Ile	Ala	Ala	Asp	Glu	
	1				5				10					15		
AGC	TTC	ACC	CAG	GTG	GAC	ATT	GGT	GAC	AGG	ATC	ATG	AAG	CTG	AAT	ACA	94
Ser	Phe	Thr	Gln	Val	Asp	Ile	Gly	Asp	Arg	Ile	Met	Lys	Leu	Asn	Thr	
				20				25						30		
GAG	GTG	CGG	GAC	GTG	GGG	CCT	CTC	AGC	AAG	AAA	GGG	TTT	TAC	TTG	GCT	142
Glu	Val	Arg	Asp	Val	Gly	Pro	Leu	Ser	Lys	Lys	Gly	Phe	Tyr	Leu	Ala	
			35					40					45			
TTC	CAG	GAC	GTC	GGT	GCC	TGC	ATT	GCT	TTG	GTG	TCT	GTT	CGT	GTC	TTC	190
Phe	Gln	Asp	Val	Gly	Ala	Cys	Ile	Ala	Leu	Val	Ser	Val	Arg	Val	Phe	
		50					55					60				
TAT	AAG	AAG	TGC	CCA	CTG	ACA	GTT	CGA	AAC	CTG	GCA	CAG	TTT	CCA	GAC	238
Tyr	Lys	Lys	Cys	Pro	Leu	Thr	Val	Arg	Asn	Leu	Ala	Gln	Phe	Pro	Asp	
	65					70					75					
ACC	ATT	ACT	GGG	GCT	GAT	ACA	TCC	TCT	CTG	GTG	GAG	GTT	CGT	GGC	TCC	286
Thr	Ile	Thr	Gly	Ala	Asp	Thr	Ser	Ser	Leu	Val	Glu	Val	Arg	Gly	Ser	
	80				85					90				95		
TGT	GTC	AAC	AAC	TCG	GAA	GAG	AAG	GAC	GTG	CCA	AAA	ATG	TAC	TGC	GGG	334
Cys	Val	Asn	Asn	Ser	Glu	Glu	Lys	Asp	Val	Pro	Lys	Met	Tyr	Cys	Gly	
				100					105					110		
GCA	GAT	GGT	GAA	TGG	CTG	GTA	CCC	ATT	GGC	AAC	TGT	CTG	TGC	AAT	GCT	382
Ala	Asp	Gly	Glu	Trp	Leu	Val	Pro	Ile	Gly	Asn	Cys	Leu	Cys	Asn	Ala	
			115					120					125			
GGC	TAT	GAA	GAA	CGC	AAT	GGT	GAA	TGC	CAA	GCT	TGC	AAA	ATC	GGA	TAC	430
Gly	Tyr	Glu	Glu	Arg	Asn	Gly	Glu	Cys	Gln	Ala	Cys	Lys	Ile	Gly	Tyr	
		130					135					140				

TAC Tyr	AAG Lys	GCG Ala	CTC Leu	TCA Ser	ACA Thr	GAT Asp	GTT Val	GCA Ala	TGT Cys	GCC Ala	AAA Lys	TGC Cys	CCG Pro	CCT Pro	CAC His	478
145						150				155						
AGC Ser	TAC Tyr	TCC Ser	ATC Ile	TGG Trp	GAA Glu	GGC Gly	TCT Ser	ACC Thr	TCC Ser	TGC Cys	ACC Thr	TGT Cys	GAT Asp	CGG Arg	GGC Gly	526
160					165					170					175	
TTC Phe	TTC Phe	CGA Arg	GCA Ala	GAA Glu	AAT Asn	GAT Asp	GCT Ala	GCA Ala	TCC Ser	ATG Met	CCC Pro	TGC Cys	ACT Thr	CGC Arg	CCT Pro	574
				180					185						190	
CCA Pro	TCC Ser	GCA Ala	CCC Pro	CAG Gln	AAC Asn	CTG Leu	ATT Ile	TCC Ser	AAC Asn	GTC Val	AAC Asn	GAG Glu	ACG Thr	TCA Ser	GTG Val	622
			195					200					205			
AAC Asn	TTG Leu	GAG Glu	TGG Trp	AGC Ser	GCC Ala	CCA Pro	CAG Gln	AAC Asn	AAG Lys	GGA Gly	GGA Gly	CGG Arg	GAC Asp	GAC Asp	ATC Ile	670
	210						215					220				
TCC Ser	TAC Tyr	AAC Asn	GTG Val	GTG Val	TGC Cys	AAG Lys	CGC Arg	TGC Cys	GGG Gly	GCA Ala	GGG Gly	GAG Glu	CCC Pro	AGC Ser	CAC His	718
	225					230					235					
TGC Cys	CGG Arg	TCC Ser	TGT Cys	GGC Gly	AGT Ser	GGT Gly	GTA Val	CAT His	TTC Phe	AGC Ser	CCC Pro	CAG Gln	CAG Gln	AAC Asn	GGG Gly	766
240				245						250					255	
CTG Leu	AAA Lys	ACC Thr	ACG Thr	AAG Lys	GTT Val	TCC Ser	ATC Ile	ACT Thr	GAC Asp	CTC Leu	CTG Leu	GCA Ala	CAC His	ACC Thr	AAC Asn	814
				260					265						270	
TAC Tyr	ACC Thr	TTT Phe	GAG Glu	GTC Val	TGG Trp	GCA Ala	GTG Val	AAT Asn	GGA Gly	GTG Val	TCC Ser	AAG Lys	CAC His	AAC Asn	CCC Pro	862
			275					280					285			
AGC Ser	CAG Gln	GAC Asp	CAA Gln	GCT Ala	GTG Val	TCG Ser	GTC Val	ACT Thr	GTG Val	ACA Thr	ACT Thr	AAC Asn	CAA Gln	GCA Ala	GCT Ala	910
		290					295					300				
CCA Pro	TCC Ser	CCA Pro	ATT Ile	GCA Ala	TTG Leu	ATC Ile	CAG Gln	GCT Ala	AAA Lys	GAG Glu	ATA Ile	ACG Thr	AGG Arg	CAC His	AGC Ser	958
	305					310					315					
GTT Val	GCC Ala	TTG Leu	GCC Ala	TGG Trp	CTG Leu	GAA Glu	CCT Pro	GAC Asp	AGG Arg	CCC Pro	AAT Asn	GGA Gly	GTC Val	ATC Ile	CTG Leu	1006
320					325					330					335	
GAG Glu	TAC Tyr	GAA Glu	GTC Val	AAG Lys	TAC Tyr	TAC Tyr	GAA Glu	AAG Lys	GAC Asp	CAA Gln	AAC Asn	GAG Glu	CGC Arg	ACG Thr	TAT Tyr	1054
				340					345						350	
CGC Arg	ATT Ile	GTG Val	AAG Lys	ACA Thr	GCC Ala	TCC Ser	AGG Arg	AAT Asn	ACT Thr	GAC Asp	ATC Ile	AAA Lys	GGT Gly	TTG Leu	AAC Asn	1102
			355					360					365			
CCC Pro	CTG Leu	ACT Thr	TCA Ser	TAT Tyr	GTA Val	TTT Phe	CAT His	GTG Val	CGG Arg	GCC Ala	AGG Arg	ACA Thr	GCA Ala	GCA Ala	GGA Gly	1150
		370					375					380				
TAC Tyr	GGA Gly	GAC Asp	TTC Phe	AGT Ser	GGG Gly	CCG Pro	TTT Phe	GAG Glu	TTC Phe	ACA Thr	ACT Thr	AAC Asn	ACA Thr	GTT Val	CCT Pro	1198
	385					390					395					
TCC Ser	CCC Pro	ATC Ile	ATT Ile	GGC Gly	GAT Asp	GGT Gly	ACC Thr	AAT Asn	CCC Pro	ACA Thr	GTG Val	CTG Leu	CTT Leu	GTT Val	TCA Ser	1246
400					405					410					415	

52

GTG GCT GGC AGT GTT GTT CTT GTG GTC ATT CTC ATT GCA GCC TTT GTC Val Ala Gly Ser Val Val Leu Val Val Ile Leu Ile Ala Ala Phe Val 420 425 430	1294
ATC AGC AGG AGG CGC AGC AAA TAC AGT AAA GCT AAG CAA GAG GCA GAT Ile Ser Arg Arg Arg Ser Lys Tyr Ser Lys Ala Lys Gln Glu Ala Asp 435 440 445	1342
GAG GAG AAA CAT TTG AAC CAA GGT GTC AGA ACA TAT GTG GAT CCT TTT Glu Glu Lys His Leu Asn Gln Gly Val Arg Thr Tyr Val Asp Pro Phe 450 455 460	1390
ACA TAT GAG GAT CCA AAT CAA GCT GTG AGG GAA TTT GCC AAA GAA ATT Thr Tyr Glu Asp Pro Asn Gln Ala Val Arg Glu Phe Ala Lys Glu Ile 465 470 475	1438
GAT GCC TCC TGC ATA AAG ATT GAG AAA GTT ATT GGT GTG GGG GAA TTT Asp Ala Ser Cys Ile Lys Ile Glu Lys Val Ile Gly Val Gly Glu Phe 480 485 490 495	1486
GGT GAA GTA TGC AGT GGA CGT CTC AAA GTT CCA GGA AAA AGA GAA ATC Gly Glu Val Cys Ser Gly Arg Leu Lys Val Pro Gly Lys Arg Glu Ile 500 505 510	1534
TGT GTG GCT ATC AAG ACT CTG AAA GCT GGT TAC ACT GAC AAA CAA CGG Cys Val Ala Ile Lys Thr Leu Lys Ala Gly Tyr Thr Asp Lys Gln Arg 515 520 525	1582
AGA GAC TTC CTG AGT GAG GCC AGC ATC ATG GGA CAA TTT GAC CAC CCC Arg Asp Phe Leu Ser Glu Ala Ser Ile Met Gly Gln Phe Asp His Pro 530 535 540	1630
AAT ATC ATC CAC TTG GAA GGC GTT GTT ACT AAA TGT AAA CCA GTA ATG Asn Ile Ile His Leu Glu Gly Val Val Thr Lys Cys Lys Pro Val Met 545 550 555	1678
ATC ATA ACT GAG TAC ATG GAG AAT GGC TCC TTG GAT GCC TTC CTC CGG Ile Ile Thr Glu Tyr Met Glu Asn Gly Ser Leu Asp Ala Phe Leu Arg 560 565 570 575	1726
AAG AAT GAT GGC AGA TTT ACA GTA ATC CAG TTG GTG GGG ATG CTT CGT Lys Asn Asp Gly Arg Phe Thr Val Ile Gln Leu Val Gly Met Leu Arg 580 585 590	1774
GGC ATC GGC TCA GGA ATG AAG TAT CTG TCT GAC ATG AGC TAT GTG CAT Gly Ile Gly Ser Gly Met Lys Tyr Leu Ser Asp Met Ser Tyr Val His 595 600 605	1822
CGG GAT CTA GCT GCT CGA AAC ATA CTG GTC AAC AGC AAC TTG GTC TGC Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser Asn Leu Val Cys 610 615 620	1870
AAA GTG TCT GAC TTT GGC ATG TCC CGT GTC CTG GAA GAT GAC CCT GAG Lys Val Ser Asp Phe Gly Met Ser Arg Val Leu Glu Asp Asp Pro Glu 625 630 635	1918
GCA GCT TAT ACC ACA CGG GGT GGC AAG ATC CCT ATC CGA TGG ACT GCA Ala Ala Tyr Thr Thr Arg Gly Gly Lys Ile Pro Ile Arg Trp Thr Ala 640 645 650 655	1966
CCA GAG GCA ATT GCC TAC CGT AAA TTT ACA TCG GCT AGT GAC GTG TGG Pro Glu Ala Ile Ala Tyr Arg Lys Phe Thr Ser Ala Ser Asp Val Trp 660 665 670	2014
AGC TAT GGC ATC GTC ATG TGG GAA GTG ATG TCC TAT GGA GAG AGA CCT Ser Tyr Gly Ile Val Met Trp Glu Val Met Ser Tyr Gly Glu Arg Pro 675 680 685	2062

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TAC	TGG	GAT	ATG	TCC	AAT	CAA	GAC	GTT	ATT	AAA	GCC	ATT	GAG	GAA	GGG	2110
Tyr	Trp	Asp	Met	Ser	Asn	Gln	Asp	Val	Ile	Lys	Ala	Ile	Glu	Glu	Gly	
		690					695					700				
TAT	CGG	TTG	CCA	CCC	CCA	ATG	GAC	TGC	CCC	ATT	GCT	CTC	CAT	CAG	CTG	2158
Tyr	Arg	Leu	Pro	Pro	Pro	Met	Asp	Cys	Pro	Ile	Ala	Leu	His	Gln	Leu	
	705					710					715					
ATG	TTA	GAC	TGC	TGG	CAG	AAG	GAA	CGC	AGC	GAC	AGA	CCT	AAA	TTT	GGA	2206
Met	Leu	Asp	Cys	Trp	Gln	Lys	Glu	Arg	Ser	Asp	Arg	Pro	Lys	Phe	Gly	
720					725					730					735	
CAG	ATT	GTC	AAC	ATG	CTG	GAC	AAA	CTC	ATC	CGC	AAC	CCT	AAC	AGC	CTG	2254
Gln	Ile	Val	Asn	Met	Leu	Asp	Lys	Leu	Ile	Arg	Asn	Pro	Asn	Ser	Leu	
			740						745					750		
AAG	AGG	ACA	GGC	AGC	GAG	AGC	TCC	AGA	CCC	AGC	ACA	GCC	CTG	CTG	GAT	2302
Lys	Arg	Thr	Gly	Ser	Glu	Ser	Ser	Arg	Pro	Ser	Thr	Ala	Leu	Leu	Asp	
			755					760					765			
CCC	AGC	TCC	CCG	GAG	TTC	TCG	GCG	GTT	GTT	TCT	GTC	AGT	GAC	TGG	CTC	2350
Pro	Ser	Ser	Pro	Glu	Phe	Ser	Ala	Val	Val	Ser	Val	Ser	Asp	Trp	Leu	
		770					775					780				
CAA	GCC	ATT	AAA	ATG	GAG	CGA	TAC	AAG	GAT	AAC	TTC	ACA	GCT	GCT	GGC	2398
Gln	Ala	Ile	Lys	Met	Glu	Arg	Tyr	Lys	Asp	Asn	Phe	Thr	Ala	Ala	Gly	
	785					790					795					
TAT	ACC	ACC	CTA	GAG	GCT	GTG	GTG	CAT	ATG	AAC	CAG	GAC	GAC	CTG	GCC	2446
Tyr	Thr	Thr	Leu	Glu	Ala	Val	Val	His	Met	Asn	Gln	Asp	Asp	Leu	Ala	
800					805				810					815		
AGG	ATC	GGG	ATC	ACT	GCC	ATC	ACA	CAC	CAG	AAC	AAG	ATC	TTG	AGC	AGC	2494
Arg	Ile	Gly	Ile	Thr	Ala	Ile	Thr	His	Gln	Asn	Lys	Ile	Leu	Ser	Ser	
				820					825					830		
GTT	CAA	GCC	ATG	CGC	AGC	CAA	ATG	CAA	CAG	ATG	CAC	GGC	AGG	ATG	GTG	2542
Val	Gln	Ala	Met	Arg	Ser	Gln	Met	Gln	Gln	Met	His	Gly	Arg	Met	Val	
		835					840					845				
CCC	GTC	TGAGCCAGTA	CTGAATAAAC	TCAAAACTCT	TGAAATTAGT	TTACCTCATC										2598
Pro	Val															
CATGCACTTT	AATTGAAGAA	CTGCACTTTT	TTTACTTCGT	CTCCTCGCCC	GTTGAAATAA											2658
AGATCTGCAG	CATTGCTTGA	TGTACAGATT	GTGGAAACCG	AGCGTGTGTT	GGGAGGGGGG											2718
CCTCCAGAAA	TGACAAGCCG	TCATTTTAAA	CCAGACCTGG	AACAAATTGT	TTCTTGGAAC											2778
ATACTTCTCT	GTTGATCAAC	GATATGTAAA	ATACATGTAT	CC												2820

## (2) INFORMATION FOR SEQ ID NO:6:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 849 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: protein

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Gly Glu Ser Gln Phe Ala Lys Ile Asp Thr Ile Ala Ala Asp Glu Ser  
 1 5 10 15

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Phe Thr Gln Val Asp Ile Gly Asp Arg Ile Met Lys Leu Asn Thr Glu  
                   20                                  25                                  30  
 Val Arg Asp Val Gly Pro Leu Ser Lys Lys Gly Phe Tyr Leu Ala Phe  
                   35                                  40                                  45  
 Gln Asp Val Gly Ala Cys Ile Ala Leu Val Ser Val Arg Val Phe Tyr  
                   50                                  55                                  60  
 Lys Lys Cys Pro Leu Thr Val Arg Asn Leu Ala Gln Phe Pro Asp Thr  
                   65                                  70                                  75                                  80  
 Ile Thr Gly Ala Asp Thr Ser Ser Leu Val Glu Val Arg Gly Ser Cys  
                                   85                                  90                                  95  
 Val Asn Asn Ser Glu Glu Lys Asp Val Pro Lys Met Tyr Cys Gly Ala  
                                   100                                  105                                  110  
 Asp Gly Glu Trp Leu Val Pro Ile Gly Asn Cys Leu Cys Asn Ala Gly  
                   115                                  120                                  125  
 Tyr Glu Glu Arg Asn Gly Glu Cys Gln Ala Cys Lys Ile Gly Tyr Tyr  
                   130                                  135                                  140  
 Lys Ala Leu Ser Thr Asp Val Ala Cys Ala Lys Cys Pro Pro His Ser  
                   145                                  150                                  155                                  160  
 Tyr Ser Ile Trp Glu Gly Ser Thr Ser Cys Thr Cys Asp Arg Gly Phe  
                                   165                                  170                                  175  
 Phe Arg Ala Glu Asn Asp Ala Ala Ser Met Pro Cys Thr Arg Pro Pro  
                   180                                  185                                  190  
 Ser Ala Pro Gln Asn Leu Ile Ser Asn Val Asn Glu Thr Ser Val Asn  
                   195                                  200                                  205  
 Leu Glu Trp Ser Ala Pro Gln Asn Lys Gly Gly Arg Asp Asp Ile Ser  
                   210                                  215                                  220  
 Tyr Asn Val Val Cys Lys Arg Cys Gly Ala Gly Glu Pro Ser His Cys  
                   225                                  230                                  235                                  240  
 Arg Ser Cys Gly Ser Gly Val His Phe Ser Pro Gln Gln Asn Gly Leu  
                                   245                                  250                                  255  
 Lys Thr Thr Lys Val Ser Ile Thr Asp Leu Leu Ala His Thr Asn Tyr  
                   260                                  265                                  270  
 Thr Phe Glu Val Trp Ala Val Asn Gly Val Ser Lys His Asn Pro Ser  
                   275                                  280                                  285  
 Gln Asp Gln Ala Val Ser Val Thr Val Thr Thr Asn Gln Ala Ala Pro  
                   290                                  295                                  300  
 Ser Pro Ile Ala Leu Ile Gln Ala Lys Glu Ile Thr Arg His Ser Val  
                   305                                  310                                  315                                  320  
 Ala Leu Ala Trp Leu Glu Pro Asp Arg Pro Asn Gly Val Ile Leu Glu  
                   325                                  330                                  335  
 Tyr Glu Val Lys Tyr Tyr Glu Lys Asp Gln Asn Glu Arg Thr Tyr Arg  
                   340                                  345                                  350  
 Ile Val Lys Thr Ala Ser Arg Asn Thr Asp Ile Lys Gly Leu Asn Pro  
                   355                                  360                                  365



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Leu Thr Ser Tyr Val Phe His Val Arg Ala Arg Thr Ala Ala Gly Tyr  
 370 375 380  
 Gly Asp Phe Ser Gly Pro Phe Glu Phe Thr Thr Asn Thr Val Pro Ser  
 385 390 395 400  
 Pro Ile Ile Gly Asp Gly Thr Asn Pro Thr Val Leu Leu Val Ser Val  
 405 410 415  
 Ala Gly Ser Val Val Leu Val Val Ile Leu Ile Ala Ala Phe Val Ile  
 420 425 430  
 Ser Arg Arg Arg Ser Lys Tyr Ser Lys Ala Lys Gln Glu Ala Asp Glu  
 435 440 445  
 Glu Lys His Leu Asn Gln Gly Val Arg Thr Tyr Val Asp Pro Phe Thr  
 450 455 460  
 Tyr Glu Asp Pro Asn Gln Ala Val Arg Glu Phe Ala Lys Glu Ile Asp  
 465 470 475 480  
 Ala Ser Cys Ile Lys Ile Glu Lys Val Ile Gly Val Gly Glu Phe Gly  
 485 490 495  
 Glu Val Cys Ser Gly Arg Leu Lys Val Pro Gly Lys Arg Glu Ile Cys  
 500 505 510  
 Val Ala Ile Lys Thr Leu Lys Ala Gly Tyr Thr Asp Lys Gln Arg Arg  
 515 520 525  
 Asp Phe Leu Ser Glu Ala Ser Ile Met Gly Gln Phe Asp His Pro Asn  
 530 535 540  
 Ile Ile His Leu Glu Gly Val Val Thr Lys Cys Lys Pro Val Met Ile  
 545 550 555 560  
 Ile Thr Glu Tyr Met Glu Asn Gly Ser Leu Asp Ala Phe Leu Arg Lys  
 565 570 575  
 Asn Asp Gly Arg Phe Thr Val Ile Gln Leu Val Gly Met Leu Arg Gly  
 580 585 590  
 Ile Gly Ser Gly Met Lys Tyr Leu Ser Asp Met Ser Tyr Val His Arg  
 595 600 605  
 Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser Asn Leu Val Cys Lys  
 610 615 620  
 Val Ser Asp Phe Gly Met Ser Arg Val Leu Glu Asp Asp Pro Glu Ala  
 625 630 635 640  
 Ala Tyr Thr Thr Arg Gly Gly Lys Ile Pro Ile Arg Trp Thr Ala Pro  
 645 650 655  
 Glu Ala Ile Ala Tyr Arg Lys Phe Thr Ser Ala Ser Asp Val Trp Ser  
 660 665 670  
 Tyr Gly Ile Val Met Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr  
 675 680 685  
 Trp Asp Met Ser Asn Gln Asp Val Ile Lys Ala Ile Glu Glu Gly Tyr  
 690 695 700  
 Arg Leu Pro Pro Pro Met Asp Cys Pro Ile Ala Leu His Gln Leu Met  
 705 710 715 720

56

Leu Asp Cys Trp Gln Lys Glu Arg Ser Asp Arg Pro Lys Phe Gly Gln  
                     725                    730                    735  
 Ile Val Asn Met Leu Asp Lys Leu Ile Arg Asn Pro Asn Ser Leu Lys  
                     740                    745                    750  
 Arg Thr Gly Ser Glu Ser Ser Arg Pro Ser Thr Ala Leu Leu Asp Pro  
                     755                    760                    765  
 Ser Ser Pro Glu Phe Ser Ala Val Val Ser Val Ser Asp Trp Leu Gln  
                     770                    775                    780  
 Ala Ile Lys Met Glu Arg Tyr Lys Asp Asn Phe Thr Ala Ala Gly Tyr  
                     785                    790                    795                    800  
 Thr Thr Leu Glu Ala Val Val His Met Asn Gln Asp Asp Leu Ala Arg  
                     805                    810                    815  
 Ile Gly Ile Thr Ala Ile Thr His Gln Asn Lys Ile Leu Ser Ser Val  
                     820                    825                    830  
 Gln Ala Met Arg Ser Gln Met Gln Gln Met His Gly Arg Met Val Pro  
                     835                    840                    845  
 Val

## (2) INFORMATION FOR SEQ ID NO:7:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 3776 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: both
- (D) TOPOLOGY: linear

## (ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 290..3208

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

CGGCTCTGAC TTTGTGTTAA CGGTTTATGG ACTGGTTCCA AAGAGCTCAA AGGTACCAAA	60
ACACTCCAAG CAACCTCTGA ACCATTCAAG CAAGTAGTGT GTGTTTATTG GATATGGTGG	120
AGTCTACAGA GAATCTTCAT GGATTCTAAT GCTGACATCA GTGCAAGAAG AGTGTCAGGA	180
ATGGATTGGC TCTGGCTGGT TTGCTTCTTT CATCTAGTCA CTTCACTAGA AGACCTGCAT	240
CCTGACCAAC CGGAAAGGTG AGCAGGATGA GGCCATTGGT GGTGCTGTC ATG ACT	295
Met Thr	
1	
GAA ATA CTT CTG GAT ACA ACT GGA GAA ACC TCA GAG ATT GGC TGG ACC	343
Glu Ile Leu Leu Asp Thr Thr Gly Glu Thr Ser Glu Ile Gly Trp Thr	
5 10 15	
TCT CAC CCT CCT GAT GGG TGG GAA GAA GTA AGT GTC CGG GAT GAT AAG	391
Ser His Pro Pro Asp Gly Trp Glu Glu Val Ser Val Arg Asp Asp Lys	
20 25 30	
GAG CGC CAG ATC CGA ACC TTT CAA GTT TGT AAC ATG GAT GAA CCA GGT	439
Glu Arg Gln Ile Arg Thr Phe Gln Val Cys Asn Met Asp Glu Pro Gly	
35 40 45 50	

57

CAG Gln	AAT Asn	AAC Asn	TGG Trp	TTG Leu	CGT Arg	ACT Thr	CAC His	TTC Phe	ATA Ile	GAG Glu	CGA Arg	CGT Arg	GGA Gly	GCC Ala	CAC His	487
				55					60					65		
CGA Arg	GTC Val	CAT His	GTC Val	CGC Arg	CTT Leu	CAT His	TTC Phe	TCA Ser	GTG Val	AGG Arg	GAC Asp	TGT Cys	GCC Ala	AGC Ser	ATG Met	535
			70					75					80			
CGT Arg	ACT Thr	GTG Val	GCC Ala	TCT Ser	ACT Thr	TGC Cys	AAA Lys	GAG Glu	ACT Thr	TTC Phe	ACA Thr	CTC Leu	TAC Tyr	TAC Tyr	CAC His	583
		85					90					95				
CAG Gln	TCA Ser	GAT Asp	GTC Val	GAC Asp	ATA Ile	GCC Ala	TCT Ser	CAG Gln	GAA Glu	CTG Leu	CCA Pro	GAG Glu	TGG Trp	CAT His	GAA Glu	631
	100					105					110					
GGC Gly	CCC Pro	TGG Trp	ACC Thr	AAG Lys	GTG Val	GAT Asp	ACT Thr	ATT Ile	GCA Ala	GCT Ala	GAT Asp	GAA Glu	AGC Ser	TTT Phe	TCC Ser	679
	115				120					125					130	
CAG Gln	GTG Val	GAC Asp	AGA Arg	ACT Thr	GGG Gly	AAG Lys	GTG Val	GTA Val	AGG Arg	ATG Met	AAT Asn	GTT Val	AAA Lys	GTA Val	CGC Arg	727
				135					140					145		
AGC Ser	TTT Phe	GGG Gly	CCA Pro	CTC Leu	ACA Thr	AAG Lys	CAT His	GGC Gly	TTC Phe	TAC Tyr	CTG Leu	GCC Ala	TTC Phe	CAG Gln	GAC Asp	775
			150					155					160			
TCA Ser	GGA Gly	GCC Ala	TGT Cys	ATG Met	TCC Ser	CTG Leu	GTG Val	GCA Ala	GTC Val	CAA Gln	GTC Val	TTT Phe	TTC Phe	TAC Tyr	AAG Lys	823
		165					170					175				
TGT Cys	CCA Pro	GCT Ala	GTG Val	GTG Val	AAA Lys	GGA Gly	TTT Phe	GCC Ala	TCC Ser	TTC Phe	CCT Pro	GAA Glu	ACT Thr	TTT Phe	GCT Ala	871
	180					185					190					
GGA Gly	GGA Gly	GAG Glu	AGG Arg	ACC Thr	TCA Ser	CTG Leu	GTG Val	GAG Glu	TCA Ser	CTA Leu	GGG Gly	ACG Thr	TGT Cys	GTA Val	GCA Ala	919
	195				200					205				210		
AAT Asn	GCT Ala	GAA Glu	GAG Glu	GCA Ala	AGC Ser	ACA Thr	ACT Thr	GGG Gly	TCA Ser	TCA Ser	GGT Gly	GTT Val	CGG Arg	TTG Leu	CAC His	967
				215				220						225		
TGC Cys	AAT Asn	GGA Gly	GAA Glu	GGA Gly	GAG Glu	TGG Trp	ATG Met	GTG Val	GCC Ala	ACT Thr	GGA Gly	CGA Arg	TGC Cys	TCT Ser	TGC Cys	1015
			230					235					240			
AAG Lys	GCT Ala	GGT Gly	TAC Tyr	CAA Gln	TCT Ser	GTT Val	GAC Asp	AAT Asn	GAG Glu	CAA Gln	GCT Ala	TGT Cys	CAA Gln	GCT Ala	TGT Cys	1063
		245					250					255				
CCC Pro	ATT Ile	GGT Gly	TCC Ser	TTT Phe	AAA Lys	GCA Ala	TCT Ser	GTG Val	GGA Gly	GAT Asp	GAC Asp	CCT Pro	TGC Cys	CTT Leu	CTC Leu	1111
	260					265					270					
TGC Cys	CCT Pro	GCC Ala	CAC His	AGC Ser	CAT His	GCT Ala	CCA Pro	CTG Leu	CCA Pro	CTG Leu	CCA Pro	GGT Gly	TCC Ser	ATT Ile	GAA Glu	1159
	275				280				285					290		
TGT Cys	GTG Val	TGT Cys	CAG Gln	AGT Ser	CAC His	TAC Tyr	TAC Tyr	CGA Arg	TCT Ser	GCT Ala	TCT Ser	GAC Asp	AAT Asn	TCT Ser	GAT Asp	1207
				295				300						305		
GCT Ala	CCC Pro	TGC Cys	ACT Thr	GGC Gly	ATC Ile	CCC Pro	TCT Ser	GCT Ala	CCC Pro	CGT Arg	GAC Asp	CTC Leu	AGT Ser	TAT Tyr	GAA Glu	1255
			310					315					320			

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ATT Ile	GTT Val	GGC Gly	TCC Ser	AAC Asn	GTG Val	CTC Leu	CTG Leu	ACC Thr	TGG Trp	CGC Arg	CTC Leu	CCC Pro	AAG Lys	GAC Asp	TTG Leu	1303
		325					330					335				
GGT Gly	GGC Gly	CGC Arg	AAG Lys	GAT Asp	GTC Val	TTC Phe	TTC Phe	AAT Asn	GTC Val	ATC Ile	TGC Cys	AAG Lys	GAA Glu	TGC Cys	CCA Pro	1351
	340					345					350					
ACA Thr	AGG Arg	TCA Ser	GCA Ala	GGG Gly	ACA Thr	TGT Cys	GTG Val	CGC Arg	TGT Cys	GGG Gly	GAC Asp	AAT Asn	GTA Val	CAG Gln	TTT Phe	1399
	355				360					365					370	
GAA Glu	CCA Pro	CGC Arg	CAA Gln	GTG Val	GGC Gly	CTG Leu	ACA Thr	GAA Glu	AGT Ser	CGT Arg	GTT Val	CAA Gln	GTC Val	TCC Ser	AAC Asn	1447
				375					380					385		
CTA Leu	TTG Leu	GCC Ala	CGT Arg	GTG Val	CAG Gln	TAC Tyr	ACT Thr	TTT Phe	GAG Glu	ATC Ile	CAG Gln	GCT Ala	GTC Val	AAT Asn	TTG Leu	1495
			390					395				400				
GTG Val	ACT Thr	GAG Glu	TTG Leu	AGT Ser	TCA Ser	GAA Glu	GCA Ala	CCC Pro	CAG Gln	TAT Tyr	GCT Ala	ACC Thr	ATC Ile	AAC Asn	GTT Val	1543
		405					410					415				
AGC Ser	ACC Thr	AGC Ser	CAG Gln	TCA Ser	GTG Val	CCC Pro	TCC Ser	GCA Ala	ATC Ile	CCT Pro	ATG Met	ATG Met	CAT His	CAG Gln	GTG Val	1591
	420					425					430					
AGT Ser	CGT Arg	GCT Ala	ACC Thr	AGT Ser	AGC Ser	ATC Ile	ACA Thr	CTG Leu	TCT Ser	TGG Trp	CCT Pro	CAG Gln	CCA Pro	GAC Asp	CAG Gln	1639
	435				440					445					450	
CCC Pro	AAT Asn	GGG Gly	GTT Val	ATC Ile	CTG Leu	GAT Asp	TAC Tyr	CAG Gln	CTA Leu	CGG Arg	TAC Tyr	TTT Phe	GAC Asp	AAG Lys	GCA Ala	1687
				455				460					465			
GAA Glu	GAT Asp	GAG Glu	GAT Asp	AAT Asn	TCA Ser	TTT Phe	ACT Thr	TTG Leu	ACT Thr	AGT Ser	GAA Glu	ACT Thr	AAC Asn	ATG Met	GCC Ala	1735
		470					475					480				
ACT Thr	ATA Ile	TTA Leu	AAT Asn	CTG Leu	AGT Ser	CCA Pro	GGC Gly	AAG Lys	ATC Ile	TAT Tyr	GTC Val	TTT Phe	CAA Gln	GTA Val	CGA Arg	1783
		485				490						495				
GCT Ala	AGA Arg	ACA Thr	GCA Ala	GTG Val	GGT Gly	TAT Tyr	GGC Gly	CCA Pro	TAC Tyr	AGT Ser	GGA Gly	AAG Lys	ATG Met	TAT Tyr	TTT Phe	1831
	500				505						510					
CAG Gln	ACT Thr	TTA Leu	ATG Met	GCA Ala	GGA Gly	GAG Glu	CAC His	TCG Ser	GAG Glu	ATG Met	GCA Ala	CAG Gln	GAC Asp	CGA Arg	CTG Leu	1879
	515			520					525						530	
CCA Pro	CTT Leu	ATT Ile	GTG Val	GGC Gly	TCA Ser	GCA Ala	CTT Leu	GGT Gly	GGT Gly	CTG Leu	GCA Ala	TTC Phe	TTG Leu	GTA Val	ATT Ile	1927
				535				540						545		
GCT Ala	GCC Ala	ATT Ile	GCC Ala	ATT Ile	CTT Leu	GCC Ala	ATC Ile	ATC Ile	TTC Phe	AAG Lys	AGT Ser	AAA Lys	AGG Arg	CGA Arg	GAG Glu	1975
		550					555						560			
ACT Thr	CCA Pro	TAC Tyr	ACA Thr	GAC Asp	CGC Arg	CTG Leu	CAG Gln	CAG Gln	TAT Tyr	ATC Ile	AGT Ser	ACA Thr	CGA Arg	GGA Gly	CTT Leu	2023
		565				570						575				
GGA Gly	GTG Val	AAG Lys	TAT Tyr	TAC Tyr	ATT Ile	GAT Asp	CCT Pro	TCC Ser	ACG Thr	TAT Tyr	GAA Glu	GAT Asp	CCC Pro	AAT Asn	GAA Glu	2071
	580					585					590					

GCT ATT CGA GAG TTT GCC AAA GAG ATA GAT GTG TCC TTC ATC AAA ATT	2119
Ala Ile Arg Glu Phe Ala Lys Glu Ile Asp Val Ser Phe Ile Lys Ile	
595 600 605 610	
GAG GAG GTC ATT GGA TCA GGA GAA TTT GGA GAG GTG TGC TTT GGG CGC	2167
Glu Glu Val Ile Gly Ser Gly Glu Phe Gly Glu Val Cys Phe Gly Arg	
615 620 625	
CTA AAA CAC CCA GGG AAA CGT GAA TAC ACA GTA GCT ATT AAA ACC CTG	2215
Leu Lys His Pro Gly Lys Arg Glu Tyr Thr Val Ala Ile Lys Thr Leu	
630 635 640	
AAG TCA GGT TAT ACT GAT GAA CAG CGT CGA GAG TTC CTG AGC GAG GCC	2263
Lys Ser Gly Tyr Thr Asp Glu Gln Arg Arg Glu Phe Leu Ser Glu Ala	
645 650 655	
AGC ATC ATG GGG CAA TTT GAG CAT CCC AAT GTC ATC CAC CTG GAG GGC	2311
Ser Ile Met Gly Gln Phe Glu His Pro Asn Val Ile His Leu Glu Gly	
660 665 670	
GTG GTC ACC AAA AGC CGA CCA GTC ATG ATT GTC ACA GAA TTC ATG GAG	2359
Val Val Thr Lys Ser Arg Pro Val Met Ile Val Thr Glu Phe Met Glu	
675 680 685 690	
AAT GGA TCA CTG GAT TCC TTC CTC AGG GAG AAG GAG GGA CAG TTC AGT	2407
Asn Gly Ser Leu Asp Ser Phe Leu Arg Glu Lys Glu Gly Gln Phe Ser	
695 700 705	
GTG TTA CAG CTG GTG GGA ATG CTA CGA GGG ATT GCA GCA GGC ATG CGC	2455
Val Leu Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ala Gly Met Arg	
710 715 720	
TAC CTT TCA GAC ATG AAC TAT GTG CAT CGT GAT CTC GCA GCA CGT AAC	2503
Tyr Leu Ser Asp Met Asn Tyr Val His Arg Asp Leu Ala Ala Arg Asn	
725 730 735	
ATC TTA GTC AAC AGT AAC CTT GTA TGC AAG GTG TCA GAC TTT GGT TTG	2551
Ile Leu Val Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu	
740 745 750	
TCT CGC TTT CTG GAA GAT GAT GCT TCA AAT CCC ACT TAT ACT GGA GCT	2599
Ser Arg Phe Leu Glu Asp Asp Ala Ser Asn Pro Thr Tyr Thr Gly Ala	
755 760 765 770	
CTG GGT TGC AAA ATC CCC ATC CGT TGG ACT GCC CCT GAA GCT GTC CAG	2647
Leu Gly Cys Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala Val Gln	
775 780 785	
TAT CGC AAG TTC ACC TCC TCC AGT GAT GTC TGG AGC TAT GGC ATT GTC	2695
Tyr Arg Lys Phe Thr Ser Ser Ser Asp Val Trp Ser Tyr Gly Ile Val	
790 795 800	
ATG TGG GAG GTG ATG TCC TAT GGT GAG AGA CCT TAC TGG GAC ATG TCC	2743
Met Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Asp Met Ser	
805 810 815	
AAC CAG GAT GTA ATT AAT GCC ATT GAC CAG GAC TAT CGC CTG CCA CCA	2791
Asn Gln Asp Val Ile Asn Ala Ile Asp Gln Asp Tyr Arg Leu Pro Pro	
820 825 830	
CCC CCA GAC TGC CCA ACT GTT TTG CAT CTG CTG ATG CTT GAC TGC TGG	2839
Pro Pro Asp Cys Pro Thr Val Leu His Leu Leu Met Leu Asp Cys Trp	
835 840 845 850	
CAG AAG GAT CGA GTC CAG AGA CCA AAA TTT GAA CAA ATA GTC AGT GCC	2887
Gln Lys Asp Arg Val Gln Arg Pro Lys Phe Glu Gln Ile Val Ser Ala	
855 860 865	

60

CTA	GAT	AAA	ATG	ATC	CGC	AAG	CCA	TCT	GCT	CTC	AAA	GCC	ACT	GGC	ACT	2935
Leu	Asp	Lys	Met	Ile	Arg	Lys	Pro	Ser	Ala	Leu	Lys	Ala	Thr	Gly	Thr	
			870						875					880		
GGG	AGC	AGC	AGA	CCA	TCT	CAG	CCT	CTC	CTG	AGC	AAC	TCC	CCT	CCA	GAT	2983
Gly	Ser	Ser	Arg	Pro	Ser	Gln	Pro	Leu	Leu	Ser	Asn	Ser	Pro	Pro	Asp	
			885				890						895			
TTT	CCT	TCA	CTC	AGC	AAT	GCC	CAC	GAG	TGG	TTG	GAT	GCC	ATC	AAG	ATG	3031
Phe	Pro	Ser	Leu	Ser	Asn	Ala	His	Glu	Trp	Leu	Asp	Ala	Ile	Lys	Met	
			900				905						910			
GGT	CGT	TAC	AAG	GAG	AAT	TTT	GAC	CAG	GCT	GGT	CTG	ATT	ACA	TTT	GAT	3079
Gly	Arg	Tyr	Lys	Glu	Asn	Phe	Asp	Gln	Ala	Gly	Leu	Ile	Thr	Phe	Asp	
					920					925					930	
GTC	ATA	TCA	CGC	ATG	ACT	CTG	GAA	GAT	CTC	CAG	CGT	ATT	GGA	ATC	ACC	3127
Val	Ile	Ser	Arg	Met	Thr	Leu	Glu	Asp	Leu	Gln	Arg	Ile	Gly	Ile	Thr	
					935					940					945	
CTG	GTT	GGT	CAC	CAG	AAA	AAG	ATT	CTA	AAC	AGC	ATC	CAG	CTC	ATG	AAA	3175
Leu	Val	Gly	His	Gln	Lys	Lys	Ile	Leu	Asn	Ser	Ile	Gln	Leu	Met	Lys	
					950					955					960	
GTT	CAT	TTG	AAC	CAG	CTT	GAA	CCA	GTT	GAA	GTG	TGATGCTTTA	AGTCTCTATT				3228
Val	His	Leu	Asn	Gln	Leu	Glu	Pro	Val	Glu	Val						
			965							970						
TCACCAGACT	CAAATTCTGA	AAGAGTCCTG	AGGGGATTCA	GAGGGATTGT	CACTGTATGA											3288
AAAGGAAATG	GCAAGATGCT	CCTTGAAGAC	TTACTGCACC	TAGAGAGTAG	ACATTACACA											3348
TTCCATTCCA	CCAGCAAAAA	GAGAATCTTG	CCATCATTTA	AAAGCAGAGT	TAAATAGCTG											3408
GTGGTTAAAT	ATGACTGGCA	TCATACACTA	GGAGTAGGTC	AGGGAGGGAA	AGTTATAGTA											3468
ATGCAGAGTG	GAGCTGGTAT	AATAGTTTGG	ACAGACCACA	AGCACCTGCT	AGCTCTTCTC											3528
CACTAAATAA	AAAATCAGAC	AATTCTCCAG	TGCCATCAGC	AGGCTTTTATC	TGTGACTGGG											3588
AACAAAGAAA	TCACAATTTT	TCCAAGAGAG	TATCAGCACA	TTGTGAGAGT	TATCACTCAG											3648
TTGGAAATGG	ACATCACTTG	CTATGCCAGA	TTTGTGAGAA	ACTGGAGTTC	CACTGAGTGC											3708
ACCATATGTG	GTAAACAATA	AGGTACATCA	CCTCGTAATT	TTTACAGAGG	TTGAGAGTAA											3768
AGGGCCCA																3776

## (2) INFORMATION FOR SEQ ID NO:8:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 973 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: protein

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

Met Thr Glu Ile Leu Leu Asp Thr Thr Gly Glu Thr Ser Glu Ile Gly  
 1 5 10 15

Trp Thr Ser His Pro Pro Asp Gly Trp Glu Glu Val Ser Val Arg Asp  
 20 25 30

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Asp Lys Glu Arg Gln Ile Arg Thr Phe Gln Val Cys Asn Met Asp Glu  
           35                                  40                                  45  
 Pro Gly Gln Asn Asn Trp Leu Arg Thr His Phe Ile Glu Arg Arg Gly  
           50                                  55                                  60  
 Ala His Arg Val His Val Arg Leu His Phe Ser Val Arg Asp Cys Ala  
   65                                  70                                  75                                  80  
 Ser Met Arg Thr Val Ala Ser Thr Cys Lys Glu Thr Phe Thr Leu Tyr  
                                   85                                  90                                  95  
 Tyr His Gln Ser Asp Val Asp Ile Ala Ser Gln Glu Leu Pro Glu Trp  
                                   100                                  105                                  110  
 His Glu Gly Pro Trp Thr Lys Val Asp Thr Ile Ala Ala Asp Glu Ser  
                                   115                                  120                                  125  
 Phe Ser Gln Val Asp Arg Thr Gly Lys Val Val Arg Met Asn Val Lys  
   130                                  135                                  140  
 Val Arg Ser Phe Gly Pro Leu Thr Lys His Gly Phe Tyr Leu Ala Phe  
   145                                  150                                  155                                  160  
 Gln Asp Ser Gly Ala Cys Met Ser Leu Val Ala Val Gln Val Phe Phe  
                                   165                                  170                                  175  
 Tyr Lys Cys Pro Ala Val Val Lys Gly Phe Ala Ser Phe Pro Glu Thr  
                                   180                                  185                                  190  
 Phe Ala Gly Gly Glu Arg Thr Ser Leu Val Glu Ser Leu Gly Thr Cys  
                                   195                                  200                                  205  
 Val Ala Asn Ala Glu Glu Ala Ser Thr Thr Gly Ser Ser Gly Val Arg  
   210                                  215                                  220  
 Leu His Cys Asn Gly Glu Gly Glu Trp Met Val Ala Thr Gly Arg Cys  
   225                                  230                                  235                                  240  
 Ser Cys Lys Ala Gly Tyr Gln Ser Val Asp Asn Glu Gln Ala Cys Gln  
                                   245                                  250                                  255  
 Ala Cys Pro Ile Gly Ser Phe Lys Ala Ser Val Gly Asp Asp Pro Cys  
                                   260                                  265                                  270  
 Leu Leu Cys Pro Ala His Ser His Ala Pro Leu Pro Leu Pro Gly Ser  
   275                                  280                                  285  
 Ile Glu Cys Val Cys Gln Ser His Tyr Tyr Arg Ser Ala Ser Asp Asn  
   290                                  295                                  300  
 Ser Asp Ala Pro Cys Thr Gly Ile Pro Ser Ala Pro Arg Asp Leu Ser  
   305                                  310                                  315                                  320  
 Tyr Glu Ile Val Gly Ser Asn Val Leu Leu Thr Trp Arg Leu Pro Lys  
                                   325                                  330                                  335  
 Asp Leu Gly Gly Arg Lys Asp Val Phe Phe Asn Val Ile Cys Lys Glu  
                                   340                                  345                                  350  
 Cys Pro Thr Arg Ser Ala Gly Thr Cys Val Arg Cys Gly Asp Asn Val  
                                   355                                  360                                  365  
 Gln Phe Glu Pro Arg Gln Val Gly Leu Thr Glu Ser Arg Val Gln Val  
   370                                  375                                  380

62

Ser	Asn	Leu	Leu	Ala	Arg	Val	Gln	Tyr	Thr	Phe	Glu	Ile	Gln	Ala	Val
385					390					395					400
Asn	Leu	Val	Thr	Glu	Leu	Ser	Ser	Glu	Ala	Pro	Gln	Tyr	Ala	Thr	Ile
				405					410					415	
Asn	Val	Ser	Thr	Ser	Gln	Ser	Val	Pro	Ser	Ala	Ile	Pro	Met	Met	His
			420					425					430		
Gln	Val	Ser	Arg	Ala	Thr	Ser	Ser	Ile	Thr	Leu	Ser	Trp	Pro	Gln	Pro
			435				440					445			
Asp	Gln	Pro	Asn	Gly	Val	Ile	Leu	Asp	Tyr	Gln	Leu	Arg	Tyr	Phe	Asp
450						455					460				
Lys	Ala	Glu	Asp	Glu	Asp	Asn	Ser	Phe	Thr	Leu	Thr	Ser	Glu	Thr	Asn
465					470					475					480
Met	Ala	Thr	Ile	Leu	Asn	Leu	Ser	Pro	Gly	Lys	Ile	Tyr	Val	Phe	Gln
				485					490					495	
Val	Arg	Ala	Arg	Thr	Ala	Val	Gly	Tyr	Gly	Pro	Tyr	Ser	Gly	Lys	Met
			500					505					510		
Tyr	Phe	Gln	Thr	Leu	Met	Ala	Gly	Glu	His	Ser	Glu	Met	Ala	Gln	Asp
		515					520					525			
Arg	Leu	Pro	Leu	Ile	Val	Gly	Ser	Ala	Leu	Gly	Gly	Leu	Ala	Phe	Leu
	530					535					540				
Val	Ile	Ala	Ala	Ile	Ala	Ile	Leu	Ala	Ile	Ile	Phe	Lys	Ser	Lys	Arg
545					550					555					560
Arg	Glu	Thr	Pro	Tyr	Thr	Asp	Arg	Leu	Gln	Gln	Tyr	Ile	Ser	Thr	Arg
				565					570					575	
Gly	Leu	Gly	Val	Lys	Tyr	Tyr	Ile	Asp	Pro	Ser	Thr	Tyr	Glu	Asp	Pro
			580					585					590		
Asn	Glu	Ala	Ile	Arg	Glu	Phe	Ala	Lys	Glu	Ile	Asp	Val	Ser	Phe	Ile
		595					600					605			
Lys	Ile	Glu	Glu	Val	Ile	Gly	Ser	Gly	Glu	Phe	Gly	Glu	Val	Cys	Phe
	610					615					620				
Gly	Arg	Leu	Lys	His	Pro	Gly	Lys	Arg	Glu	Tyr	Thr	Val	Ala	Ile	Lys
625					630					635					640
Thr	Leu	Lys	Ser	Gly	Tyr	Thr	Asp	Glu	Gln	Arg	Arg	Glu	Phe	Leu	Ser
				645					650					655	
Glu	Ala	Ser	Ile	Met	Gly	Gln	Phe	Glu	His	Pro	Asn	Val	Ile	His	Leu
			660					665					670		
Glu	Gly	Val	Val	Thr	Lys	Ser	Arg	Pro	Val	Met	Ile	Val	Thr	Glu	Phe
		675					680					685			
Met	Glu	Asn	Gly	Ser	Leu	Asp	Ser	Phe	Leu	Arg	Glu	Lys	Glu	Gly	Gln
	690					695					700				
Phe	Ser	Val	Leu	Gln	Leu	Val	Gly	Met	Leu	Arg	Gly	Ile	Ala	Ala	Gly
705					710					715					720
Met	Arg	Tyr	Leu	Ser	Asp	Met	Asn	Tyr	Val	His	Arg	Asp	Leu	Ala	Ala
				725					730					735	



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Arg Asn Ile Leu Val Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe  
                     740                    745                    750  
 Gly Leu Ser Arg Phe Leu Glu Asp Asp Ala Ser Asn Pro Thr Tyr Thr  
                     755                    760                    765  
 Gly Ala Leu Gly Cys Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala  
                     770                    775                    780  
 Val Gln Tyr Arg Lys Phe Thr Ser Ser Ser Asp Val Trp Ser Tyr Gly  
                     785                    790                    795                    800  
 Ile Val Met Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Asp  
                     805                    810                    815  
 Met Ser Asn Gln Asp Val Ile Asn Ala Ile Asp Gln Asp Tyr Arg Leu  
                     820                    825                    830  
 Pro Pro Pro Pro Asp Cys Pro Thr Val Leu His Leu Leu Met Leu Asp  
                     835                    840                    845  
 Cys Trp Gln Lys Asp Arg Val Gln Arg Pro Lys Phe Glu Gln Ile Val  
                     850                    855                    860  
 Ser Ala Leu Asp Lys Met Ile Arg Lys Pro Ser Ala Leu Lys Ala Thr  
                     865                    870                    875                    880  
 Gly Thr Gly Ser Ser Arg Pro Ser Gln Pro Leu Leu Ser Asn Ser Pro  
                     885                    890                    895  
 Pro Asp Phe Pro Ser Leu Ser Asn Ala His Glu Trp Leu Asp Ala Ile  
                     900                    905                    910  
 Lys Met Gly Arg Tyr Lys Glu Asn Phe Asp Gln Ala Gly Leu Ile Thr  
                     915                    920                    925  
 Phe Asp Val Ile Ser Arg Met Thr Leu Glu Asp Leu Gln Arg Ile Gly  
                     930                    935                    940  
 Ile Thr Leu Val Gly His Gln Lys Lys Ile Leu Asn Ser Ile Gln Leu  
                     945                    950                    955                    960  
 Met Lys Val His Leu Asn Gln Leu Glu Pro Val Glu Val  
                     965                    970

## (2) INFORMATION FOR SEQ ID NO:9:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 3546 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: both
- (D) TOPOLOGY: linear

## (ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 2..2920

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

C GGG GTC TCC TCG AGG GCG CGG CCG CCG GGC AGC AGC AGG AGC  
 Gly Val Ser Ser Arg Ala Arg Arg Pro Pro Gly Ser Ser Arg Ser  
 1                    5                    10                    15

46

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AGC Ser	AGG Arg	AGG Arg	GGG Gly	GTG Val	ACC Thr	TCG Ser	GAG Glu	CTG Leu	GCA Ala	TGG Trp	ACA Thr	ACC Thr	CAT His	CCG Pro	GAG Glu	94
				20					25					30		
ACG Thr	GGG Gly	TGG Trp	GAA Glu	GAG Glu	GTC Val	AGT Ser	GGT Gly	TAC Tyr	GAC Asp	GAG Glu	GCT Ala	ATG Met	AAC Asn	CCC Pro	ATC Ile	142
			35					40					45			
CGC Arg	ACA Thr	TAC Tyr	CAG Gln	GTG Val	TGC Cys	AAC Asn	GTG Val	CGG Arg	GAG Glu	GCC Ala	AAC Asn	CAG Gln	AAC Asn	AAC Asn	TGG Trp	190
		50					55					60				
CTT Leu	CGC Arg	ACC Thr	AAG Lys	TTC Phe	ATT Ile	CAG Gln	CGC Arg	CAG Gln	GAC Asp	GTC Val	CAG Gln	CGT Arg	GTC Val	TAC Tyr	GTG Val	238
	65					70					75					
GAG Glu	CTG Leu	AAA Lys	TTC Phe	ACT Thr	GTG Val	CGG Arg	GAC Asp	TGC Cys	AAC Asn	AGC Ser	ATC Ile	CCC Pro	AAC Asn	ATC Ile	CCT Pro	286
	80				85					90					95	
GGT Gly	TCC Ser	TGC Cys	AAA Lys	GAG Glu	ACC Thr	TTC Phe	AAC Asn	CTC Leu	TTC Phe	TAT Tyr	TAT Tyr	GAG Glu	TCA Ser	GAT Asp	ACG Thr	334
				100					105					110		
GAT Asp	TCT Ser	GCC Ala	TCT Ser	GCC Ala	AAT Asn	AGC Ser	CCT Pro	TTC Phe	TGG Trp	ATG Met	GAG Glu	AAC Asn	CCC Pro	TAT Tyr	ATC Ile	382
			115					120					125			
AAA Lys	GTG Val	GAT Asp	ACA Thr	ATT Ile	GCT Ala	CCG Pro	GAT Asp	GAG Glu	AGC Ser	TTC Phe	TCC Ser	AAA Lys	CTG Leu	GAG Glu	TCC Ser	430
		130					135					140				
GGC Gly	CGT Arg	GTG Val	AAC Asn	ACC Thr	AAG Lys	GTG Val	CGC Arg	AGC Ser	TTT Phe	GGG Gly	CCG Pro	CTC Leu	TCC Ser	AAG Lys	AAT Asn	478
	145					150					155					
GGC Gly	TTT Phe	TAT Tyr	CTG Leu	GCT Ala	TTC Phe	CAG Gln	GAC Asp	CTG Leu	GGG Gly	GCC Ala	TGC Cys	ATG Met	TCC Ser	CTT Leu	ATC Ile	526
	160				165					170					175	
TCC Ser	GTC Val	CGG Arg	GCT Ala	TTC Phe	TAC Tyr	AAG Lys	AAA Lys	TGT Cys	TCC Ser	AAC Asn	ACC Thr	ATC Ile	GCT Ala	GGC Gly	TTT Phe	574
				180					185					190		
GCT Ala	ATC Ile	TTC Phe	CCG Pro	GAG Glu	ACC Thr	CTA Leu	ACG Thr	GGG Gly	GCT Ala	GAG Glu	CCC Pro	ACG Thr	TCG Ser	CTG Leu	GTC Val	622
			195					200					205			
ATT Ile	GCG Ala	CCG Pro	GGC Gly	ACC Thr	TGC Cys	ATC Ile	CCC Pro	AAC Asn	GCA Ala	GTG Val	GAA Glu	GTG Val	TCT Ser	GTG Val	CCC Pro	670
		210					215					220				
CTG Leu	AAG Lys	CTG Leu	TAC Tyr	TGC Cys	AAC Asn	GGT Gly	GAT Asp	GGC Gly	GAG Glu	TGG Trp	ATG Met	GTG Val	CCT Pro	GTG Val	GGA Gly	718
	225					230					235					
GCG Ala	TGC Cys	ACG Thr	TGT Cys	GCT Ala	GCT Ala	GGG Gly	TAC Tyr	GAG Glu	CCA Pro	GCC Ala	ATG Met	AAG Lys	GAT Asp	ACC Thr	CAG Gln	766
	240				245					250					255	
TGC Cys	CAA Gln	GCA Ala	TGC Cys	GGC Gly	CCG Pro	GGG Gly	ACG Thr	TTC Phe	AAA Lys	TCC Ser	AAG Lys	CAG Gln	GGC Gly	GAG Glu	GGC Gly	814
				260					265					270		
CCC Pro	TGC Cys	TCC Ser	CCC Pro	TGC Cys	CCT Pro	CCC Pro	AAC Asn	AGC Ser	CGC Arg	ACC Thr	ACC Thr	GCG Ala	GGG Gly	GCA Ala	GCC Ala	862
			275					280					285			

65

ACA	GTC	TGC	ATA	TGT	CGC	AGC	GGC	TTC	TTC	CGA	GCA	GAC	GCG	GAC	CCC	910
Thr	Val	Cys	Ile	Cys	Arg	Ser	Gly	Phe	Phe	Arg	Ala	Asp	Ala	Asp	Pro	
		290					295					300				
GCA	GAC	AGC	GCC	TGC	ACC	AGT	GTG	CCC	TCA	GCC	CCA	CGC	AGC	GTC	ATC	958
Ala	Asp	Ser	Ala	Cys	Thr	Ser	Val	Pro	Ser	Ala	Pro	Arg	Ser	Val	Ile	
	305					310				315						
TCC	AAC	GTG	AAT	GAG	ACG	TCG	TTG	GTG	CTG	GAG	TGG	AGC	GAG	CCG	CAG	1006
Ser	Asn	Val	Asn	Glu	Thr	Ser	Leu	Val	Leu	Glu	Trp	Ser	Glu	Pro	Gln	
	320				325					330					335	
GAC	GCG	GGC	GGG	CGG	GAT	GAC	CTG	CTC	TAC	AAC	GTC	ATC	TGC	AAG	AAG	1054
Asp	Ala	Gly	Gly	Arg	Asp	Asp	Leu	Leu	Tyr	Asn	Val	Ile	Cys	Lys	Lys	
				340					345					350		
TGC	AGC	GTG	GAG	CGG	CGG	CTG	TGC	AGC	CGC	TGC	GAC	GAC	AAC	GTG	GAG	1102
Cys	Ser	Val	Glu	Arg	Arg	Leu	Cys	Ser	Arg	Cys	Asp	Asp	Asn	Val	Glu	
			355					360					365			
TTC	GTG	CCG	CGC	CAG	CTG	GGC	CTC	ACT	GGC	CTC	ACT	GAG	CGA	CGC	ATC	1150
Phe	Val	Pro	Arg	Gln	Leu	Gly	Leu	Thr	Gly	Leu	Thr	Glu	Arg	Arg	Ile	
		370				375						380				
TAC	ATC	AGC	AAG	GTG	ATG	GCC	CAC	CCC	CAG	TAC	ACC	TTC	GAG	ATC	CAG	1198
Tyr	Ile	Ser	Lys	Val	Met	Ala	His	Pro	Gln	Tyr	Thr	Phe	Glu	Ile	Gln	
	385					390				395						
GCG	GTG	AAT	GGC	ATC	TCC	AGC	AAG	AGC	CCC	TAC	CCT	CCC	CAT	TTT	GCC	1246
Ala	Val	Asn	Gly	Ile	Ser	Ser	Lys	Ser	Pro	Tyr	Pro	Pro	His	Phe	Ala	
	400				405					410					415	
TCC	GTC	AAC	ATC	ACG	ACC	AAC	CAG	GCA	GCC	CCA	TCT	GCC	GTG	CCC	ACC	1294
Ser	Val	Asn	Ile	Thr	Thr	Asn	Gln	Ala	Ala	Pro	Ser	Ala	Val	Pro	Thr	
				420					425					430		
ATG	CAT	CTG	CAC	AGC	AGC	ACC	GGG	AAC	AGC	ATG	ACA	CTG	TCA	TGG	ACT	1342
Met	His	Leu	His	Ser	Ser	Thr	Gly	Asn	Ser	Met	Thr	Leu	Ser	Trp	Thr	
			435					440					445			
CCC	CCG	GAA	AGG	CCC	AAC	GGC	ATC	ATT	CTC	GAC	TAT	GAA	ATC	AAG	TAC	1390
Pro	Pro	Glu	Arg	Pro	Asn	Gly	Ile	Ile	Leu	Asp	Tyr	Glu	Ile	Lys	Tyr	
		450					455					460				
TCC	GAG	AAG	CAA	GGC	CAG	GGT	GAC	GGC	ATT	GCC	AAC	ACT	GTC	ACC	AGC	1438
Ser	Glu	Lys	Gln	Gly	Gln	Gly	Asp	Gly	Ile	Ala	Asn	Thr	Val	Thr	Ser	
	465					470					475					
CAG	AAG	AAC	TCG	GTG	CGG	CTG	GAC	GGA	CTG	AAG	GCC	AAT	GCT	CGG	TAC	1486
Gln	Lys	Asn	Ser	Val	Arg	Leu	Asp	Gly	Leu	Lys	Ala	Asn	Ala	Arg	Tyr	
	480				485					490					495	
ATG	GTG	CAG	GTC	CGG	GCG	CGC	ACA	GTG	GCT	GGA	TAC	GGC	CGC	TAC	AGC	1534
Met	Val	Gln	Val	Arg	Ala	Arg	Thr	Val	Ala	Gly	Tyr	Gly	Arg	Tyr	Ser	
				500					505					510		
CTC	CCC	ACC	GAG	TTC	CAG	ACG	ACT	GCG	GAG	GAT	GGC	TCC	ACC	AGC	AAG	1582
Leu	Pro	Thr	Glu	Phe	Gln	Thr	Thr	Ala	Glu	Asp	Gly	Ser	Thr	Ser	Lys	
			515					520					525			
ACT	TTC	CAG	GAG	CTT	CCT	CTC	ATC	GTG	GGT	TCA	GCC	ACC	GCG	GGA	CTG	1630
Thr	Phe	Gln	Glu	Leu	Pro	Leu	Ile	Val	Gly	Ser	Ala	Thr	Ala	Gly	Leu	
		530					535					540				
CTG	TTT	GTC	ATC	GTG	GTG	GTC	ATC	ATC	GCT	ATT	GTC	TGC	TTC	AGG	AAG	1678
Leu	Phe	Val	Ile	Val	Val	Val	Ile	Ile	Ala	Ile	Val	Cys	Phe	Arg	Lys	
	545					550					555					

66

CAG Gln 560	CGC Arg	AAC Asn	AGC Ser	ACA Thr	GAT Asp 565	CCC Pro	GAG Glu	TAC Tyr	ACA Thr	GAG Glu 570	AAG Lys	CTG Leu	CAG Gln	CAA Gln	TAT Tyr 575	1726
GTC Val	ACT Thr	CCT Pro	GGG Gly	ATG Met 580	AAG Lys	GTC Val	TAC Tyr	ATT Ile	GAC Asp 585	CCC Pro	TTC Phe	ACC Thr	TAT Tyr	GAA Glu 590	GAC Asp	1774
CCA Pro	AAT Asn	GAA Glu	GCT Ala 595	GTC Val	CGG Arg	GAA Glu	TTC Phe	GCC Ala 600	AAA Lys	GAG Glu	ATT Ile	GAT Asp	ATC Ile 605	TCC Ser	TGT Cys	1822
GTC Val	AAA Lys	ATT Ile 610	GAG Glu	GAG Glu	GTC Val	ATT Ile	GGA Gly 615	GCA Ala	GGA Gly	GAG Glu	TTT Phe	GGT Gly 620	GAG Glu	GTG Val	TGC Cys	1870
CGT Arg 625	GGG Arg	CTG Leu	AAG Lys	CTG Leu	CCT Pro 630	GGC Gly	CGC Arg	CGT Arg	GAG Glu 635	ATC Ile	TTT Phe	GTG Val	GCC Ala	ATC Ile		1918
AAG Lys 640	ACA Thr	CTG Leu	AAG Lys	GTG Val	GGC Gly 645	TAC Tyr	ACA Thr	GAG Glu	AGG Arg	CAG Gln 650	CGG Arg	CGG Arg	GAC Asp	TTC Phe	CTG Leu 655	1966
AGT Ser	GAG Glu	GCC Ala	AGC Ser	ATC Ile 660	ATG Met	GGC Gly	CAG Gln	TTC Phe	GAC Asp 665	CAC His	CCC Pro	AAC Asn	ATC Ile 670	ATC Ile	CAC His	2014
CTG Leu	GAG Glu	GGC Gly	GTG Val 675	GTG Val	ACC Thr	AAG Lys	AGC Ser	CGC Arg 680	CCT Pro	GTC Val	ATG Met	ATC Ile 685	ATC Ile	ACA Thr	GAG Glu	2062
TTC Phe	ATG Met	GAG Glu 690	AAC Asn	TGC Cys	GCT Ala	CTC Leu	GAC Asp 695	TCC Ser	TTC Phe	CTC Leu	CGG Arg	CTG Leu 700	AAT Asn	GAT Asp	GGG Gly	2110
CAG Gln 705	TTC Phe	ACG Thr	GTC Val	ATC Ile	CAG Gln 710	CTG Leu	GTG Val	GGG Gly	ATG Met	CTG Leu	CGA Arg 715	GGC Gly	ATC Ile	GCT Ala	GCT Ala	2158
GGC Gly 720	ATG Met	AAG Lys	TAC Tyr	CTC Leu	TCA Ser 725	GAG Glu	ATG Met	AAC Asn	TAC Tyr	GTG Val 730	CAC His	CGA Arg	GAC Asp	CTG Leu	GCT Ala 735	2206
GCC Ala	CGC Arg	AAC Asn	ATC Ile	CTG Leu 740	GTC Val	AAC Asn	AGC Ser	AAC Asn	TTG Leu 745	GTC Val	TGC Cys	AAA Lys	GTG Val	TCT Ser	GAC Asp 750	2254
TTC Phe	GGG Gly	CTC Leu	TCC Ser 755	CGC Arg	TTT Phe	TTG Leu	GAG Glu	GAT Asp 760	GAT Asp	CCA Pro	GCC Ala	GAC Asp	CCC Pro	ACC Thr	TAC Tyr	2302
ACC Thr	AGC Ser	TCC Ser 770	CTG Leu	GGA Gly	GGC Gly	AAG Lys	ATC Ile 775	CCC Pro	ATC Ile	AGG Arg	TGG Trp	ACA Thr 780	GCT Ala	CCT Pro	GAG Glu	2350
GCC Ala 785	ATC Ile	GCC Ala	TAC Tyr	CGC Arg	AAA Lys	TTC Phe 790	ACG Thr	TCG Ser	GCC Ala	AGC Ser	GAC Asp 795	GTG Val	TGG Trp	AGC Ser	TAC Tyr	2398
GGC Gly 800	ATC Ile	GTC Val	ATG Met	TGG Trp	GAA Glu 805	GTG Val	ATG Met	TCC Ser	TAC Tyr	GGG Gly 810	GAG Glu	CGA Arg	CCC Pro	TAC Tyr	TGG Trp 815	2446
GAC Asp	ATG Met	TCC Ser	AAC Asn	CAG Gln 820	GAT Asp	GTG Val	ATC Ile	AAC Asn	GCG Ala 825	GTG Val	GAG Glu	CAG Gln	GAT Asp	TAC Tyr	CGC Arg 830	2494

67

CTG CCA CCC CCC ATG GAC TGC CCC ACA GCA CTG CAC CAG CTG ATG CTG Leu Pro Pro Pro Met Asp Cys Pro Thr Ala Leu His Gln Leu Met Leu 835 840 845	2542
GAC TGC TGG GTG CGG GAC CGC AAC CTG CGG CCC AAG TTT GCA CAG ATT Asp Cys Trp Val Arg Asp Arg Asn Leu Arg Pro Lys Phe Ala Gln Ile 850 855 860	2590
GTC AAC ACG CTG GAC AAG CTG ATC CGC AAT GCT GCC AGC CTG AAG GTC Val Asn Thr Leu Asp Lys Leu Ile Arg Asn Ala Ala Ser Leu Lys Val 865 870 875	2638
ATC GCC AGC GTC CAG TCC GGT GTC TCC CAG CCG CTC CTG GAC CGC ACC Ile Ala Ser Val Gln Ser Gly Val Ser Gln Pro Leu Leu Asp Arg Thr 880 885 890 895	2686
GTG CCC GAT TAC ACC ACC TTC ACC ACC GTG GGA GAC TGG CTG GAT GCC Val Pro Asp Tyr Thr Thr Phe Thr Thr Val Gly Asp Trp Leu Asp Ala 900 905 910	2734
ATC AAA ATG GGA CGG TAC AAG GAG AAC TTC GTC AAC GCC GGC TTC GCC Ile Lys Met Gly Arg Tyr Lys Glu Asn Phe Val Asn Ala Gly Phe Ala 915 920 925	2782
TCC TTT GAC CTG GTG GCA CAG ATG ACA GCA GAG GAC CTG CTA AGG ATA Ser Phe Asp Leu Val Ala Gln Met Thr Ala Glu Asp Leu Leu Arg Ile 930 935 940	2830
GGA GTG ACG CTA GCA GGG CAC CAG AAG AAG ATC CTG AGC AGC ATT CAG Gly Val Thr Leu Ala Gly His Gln Lys Lys Ile Leu Ser Ser Ile Gln 945 950 955	2878
GAC ATG AGG CTG CAG ATG AAC CAG ACG CTG CCG GTT CAG GTT Asp Met Arg Leu Gln Met Asn Gln Thr Leu Pro Val Gln Val 960 965 970	2920
TGACCGCAGG GACTCTGCAT TGGAACGGAC TGAGGGAACC TGCCAACCAG GTTCTGTTTG	2980
CGGTGCAGCC CGGCTTCCCG ATTTCCCCTT CCCGTGGCGC TCCTCTGCCT CGGACGCTCG	3040
CCGGGGACAG GCTGGGCCGG GCCACCCTTC CCTGGATCAG AGGCACTCGT GCCGGGAGGG	3100
AGCCCGGCTT TTCGTCCCGT GTCCCGCAGC GGCGAGGCAG TGAACGCAGT CTTCATATTG	3160
AAGATGGATT ATGGGACGGA GATGGCGCAT CCGCTTCCCG CCCTGTCTCA GTGCTCATCA	3220
GTTTGAAGAG ATGTTCTGCT TCTTGGATTT CTTTACACCC CGGTTTTCCC CCCTCGAGTC	3280
CTCACTTCCC CCTATCCCTG AGGCCACAGA CTGTTGACCC GTCCGCTGAG TCCGTCAGAC	3340
GCTCCGAAGC CTTCCCCGAG CCCGGTCCCC GCGTGGAGAC GGCGCCAGGG ACGGGGCTAC	3400
GGCCCCAGAC AATCACTCCA CCCCTCCGCA CGAGGGTCCT CACTGGGACG TGTCTGAAGG	3460
GGAAAGGCTC TGCTCCCTTT TTGGCTTTGC ACGCCAGAAC CCGAACCCCG TGAGATTTAC	3520
TATGCAGGGA GTTAGGCAAA AAAAAG	3546

## (2) INFORMATION FOR SEQ ID NO:10:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 973 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: protein

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

Gly Val Ser Ser Arg Ala Arg Arg Pro Pro Gly Ser Ser Arg Ser Ser  
 1 5 10 15  
 Arg Arg Gly Val Thr Ser Glu Leu Ala Trp Thr Thr His Pro Glu Thr  
 20 25 30  
 Gly Trp Glu Glu Val Ser Gly Tyr Asp Glu Ala Met Asn Pro Ile Arg  
 35 40 45  
 Thr Tyr Gln Val Cys Asn Val Arg Glu Ala Asn Gln Asn Asn Trp Leu  
 50 55 60  
 Arg Thr Lys Phe Ile Gln Arg Gln Asp Val Gln Arg Val Tyr Val Glu  
 65 70 75 80  
 Leu Lys Phe Thr Val Arg Asp Cys Asn Ser Ile Pro Asn Ile Pro Gly  
 85 90 95  
 Ser Cys Lys Glu Thr Phe Asn Leu Phe Tyr Tyr Glu Ser Asp Thr Asp  
 100 105 110  
 Ser Ala Ser Ala Asn Ser Pro Phe Trp Met Glu Asn Pro Tyr Ile Lys  
 115 120 125  
 Val Asp Thr Ile Ala Pro Asp Glu Ser Phe Ser Lys Leu Glu Ser Gly  
 130 135 140  
 Arg Val Asn Thr Lys Val Arg Ser Phe Gly Pro Leu Ser Lys Asn Gly  
 145 150 155 160  
 Phe Tyr Leu Ala Phe Gln Asp Leu Gly Ala Cys Met Ser Leu Ile Ser  
 165 170 175  
 Val Arg Ala Phe Tyr Lys Lys Cys Ser Asn Thr Ile Ala Gly Phe Ala  
 180 185 190  
 Ile Phe Pro Glu Thr Leu Thr Gly Ala Glu Pro Thr Ser Leu Val Ile  
 195 200 205  
 Ala Pro Gly Thr Cys Ile Pro Asn Ala Val Glu Val Ser Val Pro Leu  
 210 215 220  
 Lys Leu Tyr Cys Asn Gly Asp Gly Glu Trp Met Val Pro Val Gly Ala  
 225 230 235 240  
 Cys Thr Cys Ala Ala Gly Tyr Glu Pro Ala Met Lys Asp Thr Gln Cys  
 245 250 255  
 Gln Ala Cys Gly Pro Gly Thr Phe Lys Ser Lys Gln Gly Glu Gly Pro  
 260 265 270  
 Cys Ser Pro Cys Pro Pro Asn Ser Arg Thr Thr Ala Gly Ala Ala Thr  
 275 280 285  
 Val Cys Ile Cys Arg Ser Gly Phe Phe Arg Ala Asp Ala Asp Pro Ala  
 290 295 300  
 Asp Ser Ala Cys Thr Ser Val Pro Ser Ala Pro Arg Ser Val Ile Ser  
 305 310 315 320  
 Asn Val Asn Glu Thr Ser Leu Val Leu Glu Trp Ser Glu Pro Gln Asp  
 325 330 335  
 Ala Gly Gly Arg Asp Asp Leu Leu Tyr Asn Val Ile Cys Lys Lys Cys  
 340 345 350

Ser Val Glu Arg Arg Leu Cys Ser Arg Cys Asp Asp Asn Val Glu Phe  
 355 360 365  
 Val Pro Arg Gln Leu Gly Leu Thr Gly Leu Thr Glu Arg Arg Ile Tyr  
 370 375 380  
 Ile Ser Lys Val Met Ala His Pro Gln Tyr Thr Phe Glu Ile Gln Ala  
 385 390 395 400  
 Val Asn Gly Ile Ser Ser Lys Ser Pro Tyr Pro Pro His Phe Ala Ser  
 405 410 415  
 Val Asn Ile Thr Thr Asn Gln Ala Ala Pro Ser Ala Val Pro Thr Met  
 420 425 430  
 His Leu His Ser Ser Thr Gly Asn Ser Met Thr Leu Ser Trp Thr Pro  
 435 440 445  
 Pro Glu Arg Pro Asn Gly Ile Ile Leu Asp Tyr Glu Ile Lys Tyr Ser  
 450 455 460  
 Glu Lys Gln Gly Gln Gly Asp Gly Ile Ala Asn Thr Val Thr Ser Gln  
 465 470 475 480  
 Lys Asn Ser Val Arg Leu Asp Gly Leu Lys Ala Asn Ala Arg Tyr Met  
 485 490 495  
 Val Gln Val Arg Ala Arg Thr Val Ala Gly Tyr Gly Arg Tyr Ser Leu  
 500 505 510  
 Pro Thr Glu Phe Gln Thr Thr Ala Glu Asp Gly Ser Thr Ser Lys Thr  
 515 520 525  
 Phe Gln Glu Leu Pro Leu Ile Val Gly Ser Ala Thr Ala Gly Leu Leu  
 530 535 540  
 Phe Val Ile Val Val Val Ile Ile Ala Ile Val Cys Phe Arg Lys Gln  
 545 550 555 560  
 Arg Asn Ser Thr Asp Pro Glu Tyr Thr Glu Lys Leu Gln Gln Tyr Val  
 565 570 575  
 Thr Pro Gly Met Lys Val Tyr Ile Asp Pro Phe Thr Tyr Glu Asp Pro  
 580 585 590  
 Asn Glu Ala Val Arg Glu Phe Ala Lys Glu Ile Asp Ile Ser Cys Val  
 595 600 605  
 Lys Ile Glu Glu Val Ile Gly Ala Gly Glu Phe Gly Glu Val Cys Arg  
 610 615 620  
 Gly Arg Leu Lys Leu Pro Gly Arg Arg Glu Ile Phe Val Ala Ile Lys  
 625 630 635 640  
 Thr Leu Lys Val Gly Tyr Thr Glu Arg Gln Arg Arg Asp Phe Leu Ser  
 645 650 655  
 Glu Ala Ser Ile Met Gly Gln Phe Asp His Pro Asn Ile Ile His Leu  
 660 665 670  
 Glu Gly Val Val Thr Lys Ser Arg Pro Val Met Ile Ile Thr Glu Phe  
 675 680 685  
 Met Glu Asn Cys Ala Leu Asp Ser Phe Leu Arg Leu Asn Asp Gly Gln  
 690 695 700

70

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Phe Thr Val Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ala Gly
705              710              715              720
Met Lys Tyr Leu Ser Glu Met Asn Tyr Val His Arg Asp Leu Ala Ala
              725              730              735
Arg Asn Ile Leu Val Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe
              740              745              750
Gly Leu Ser Arg Phe Leu Glu Asp Asp Pro Ala Asp Pro Thr Tyr Thr
              755              760              765
Ser Ser Leu Gly Gly Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala
              770              775              780
Ile Ala Tyr Arg Lys Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly
785              790              795              800
Ile Val Met Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Asp
              805              810              815
Met Ser Asn Gln Asp Val Ile Asn Ala Val Glu Gln Asp Tyr Arg Leu
              820              825              830
Pro Pro Pro Met Asp Cys Pro Thr Ala Leu His Gln Leu Met Leu Asp
              835              840              845
Cys Trp Val Arg Asp Arg Asn Leu Arg Pro Lys Phe Ala Gln Ile Val
              850              855              860
Asn Thr Leu Asp Lys Leu Ile Arg Asn Ala Ala Ser Leu Lys Val Ile
865              870              875              880
Ala Ser Val Gln Ser Gly Val Ser Gln Pro Leu Leu Asp Arg Thr Val
              885              890              895
Pro Asp Tyr Thr Thr Phe Thr Thr Val Gly Asp Trp Leu Asp Ala Ile
              900              905              910
Lys Met Gly Arg Tyr Lys Glu Asn Phe Val Asn Ala Gly Phe Ala Ser
              915              920              925
Phe Asp Leu Val Ala Gln Met Thr Ala Glu Asp Leu Leu Arg Ile Gly
              930              935              940
Val Thr Leu Ala Gly His Gln Lys Lys Ile Leu Ser Ser Ile Gln Asp
945              950              955              960
Met Arg Leu Gln Met Asn Gln Thr Leu Pro Val Gln Val
              965              970

```

## (2) INFORMATION FOR SEQ ID NO:11:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 4097 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: both
- (D) TOPOLOGY: linear

## (ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 10..3042

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:



CGGCTTCTG ATG CCC GGC CCG GAG CGC ACC ATG GGG CCG TTG TGG TTC															48
Met Pro Gly Pro Glu Arg Thr Met Gly Pro Leu Trp Phe															
1 5 10															
TGC TGT TTG CCC CTC GCC CTC TTG CCT CTG CTC GCC GCC GTG GAA GAG	96														
Cys Cys Leu Pro Leu Ala Leu Leu Pro Leu Leu Ala Ala Val Glu Glu															
15 20 25															
ACG CTG ATG GAC TCC ACA ACG GCC ACA GCA GAG CTG GGC TGG ATG GTG	144														
Thr Leu Met Asp Ser Thr Thr Ala Thr Ala Glu Leu Gly Trp Met Val															
30 35 40 45															
CAT CCT CCC TCA GGG TGG GAA GAG GTG AGT GGA TAC GAT GAG AAC ATG	192														
His Pro Pro Ser Gly Trp Glu Glu Val Ser Gly Tyr Asp Glu Asn Met															
50 55 60															
AAC ACC ATC CGC ACC TAC CAG GTG TGC AAC GTC TTT GAA TCC AGC CAA	240														
Asn Thr Ile Arg Thr Tyr Gln Val Cys Asn Val Phe Glu Ser Ser Gln															
65 70 75															
AAC AAC TGG CTG CGG ACC AAG TAC ATC CGG AGG CGA GGA GCG CAC CGC	288														
Asn Asn Trp Leu Arg Thr Lys Tyr Ile Arg Arg Arg Gly Ala His Arg															
80 85 90															
ATC CAC GTG GAG ATG AAA TTC TCC GTT CGG GAC TGC AGC AGC ATC CCC	336														
Ile His Val Glu Met Lys Phe Ser Val Arg Asp Cys Ser Ser Ile Pro															
95 100 105															
AAC GTC CCG GGC TCC TGT AAG GAG ACT TTT AAC CTC TAT TAC TAC GAA	384														
Asn Val Pro Gly Ser Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Tyr Glu															
110 115 120 125															
TCA GAC TTT GAC TCT GCC ACC AAG ACT TTT CCT AAC TGG ATG GAA AAC	432														
Ser Asp Phe Asp Ser Ala Thr Lys Thr Phe Pro Asn Trp Met Glu Asn															
130 135 140															
CCT TGG ATG AAG GTA GAT ACA ATT GCT GCC GAC GAG AGC TTC TCG CAG	480														
Pro Trp Met Lys Val Asp Thr Ile Ala Ala Asp Glu Ser Phe Ser Gln															
145 150 155															
GTG GAC CTT GGT GGG CGG GTG ATG AAG ATT AAC ACC GAG GTG CGC AGT	528														
Val Asp Leu Gly Gly Arg Val Met Lys Ile Asn Thr Glu Val Arg Ser															
160 165 170															
TTT GGG CCT GTC TCC AAA AAC GGT TTC TAC CTG GCC TTC CAG GAC TAC	576														
Phe Gly Pro Val Ser Lys Asn Gly Phe Tyr Leu Ala Phe Gln Asp Tyr															
175 180 185															
GGG GGC TGC ATG TCC TTG ATT GCA GTC CGT GTC TTT TAC CGC AAG TGT	624														
Gly Gly Cys Met Ser Leu Ile Ala Val Arg Val Phe Tyr Arg Lys Cys															
190 195 200 205															
CCC CGT GTG ATC CAG AAC GGG GCG GTC TTC CAG GAA ACC CTC TCG GGA	672														
Pro Arg Val Ile Gln Asn Gly Ala Val Phe Gln Glu Thr Leu Ser Gly															
210 215 220															
GCG GAG AGC ACA TCT CTG GTG GCA GCC CGG GGG ACG TGC ATC AGC AAT	720														
Ala Glu Ser Thr Ser Leu Val Ala Ala Arg Gly Thr Cys Ile Ser Asn															
225 230 235															
GCG GAG GAG GTG GAT GTG CCC ATC AAG CTG TAC TGC AAT GGG GAT GGC	768														
Ala Glu Glu Val Asp Val Pro Ile Lys Leu Tyr Cys Asn Gly Asp Gly															
240 245 250 255															
GAG TGG CTG GTG CCC ATC GGC CGC TGC ATG TGC AGG CCG GGC TAT GAG	816														
Glu Trp Leu Val Pro Ile Gly Arg Cys Met Cys Arg Pro Gly Tyr Glu															
255 260 265															

TCG 270	GTG Val	GAG Glu	AAT Asn	GGG Gly	ACC Thr	GTC Val	TGC Cys	AGA Arg	GGC Gly	TGC Cys	CCA Pro	TCA Ser	GGG Gly	ACC Thr	TTC Phe	864
AAG Lys	GCC Ala	AGC Ser	CAA Gln	GGA Gly	GAT Asp	GAA Glu	GGA Gly	TGT Cys	GTC Val	CAT His	TGT Cys	CCA Pro	ATT Ile	AAC Asn	AGC Ser	912
CGG Arg	ACG Thr	ACT Thr	TCG Ser	GAA Glu	GGG Gly	GCC Ala	ACG Thr	AAC Asn	TGC Cys	GTG Val	TGC Cys	CGA Arg	AAC Asn	GGA Gly	TAT Tyr	960
TAC Tyr	CGG Arg	GCA Ala	GAT Asp	GCT Ala	GAC Asp	CCC Pro	GTC Val	GAC Asp	ATG Met	CCA Pro	TGC Cys	ACC Thr	ACC Thr	ATC Ile	CCA Pro	1008
TCT Ser	GCC Ala	CCC Pro	CAG Gln	GCC Ala	GTG Val	ATC Ile	TCC Ser	AGC Ser	GTG Val	AAT Asn	GAA Glu	ACC Thr	TCC Ser	CTG Leu	ATG Met	1056
CTG 350	GAG Leu	TGG Trp	ACC Thr	CCA Pro	CCA Pro	CGA Arg	GAC Asp	TCA Ser	GGG Gly	GGC Gly	CGG Arg	GAG Glu	GAT Asp	CTG Leu	GTA Val	1104
TAC Tyr	AAC Asn	ATC Ile	ATC Ile	TGC Cys	AAG Lys	AGC Ser	TGT Cys	GGG Gly	TCA Ser	GGC Gly	CGT Arg	GGG Gly	GCG Ala	TGC Cys	ACG Thr	1152
CGC Arg	TGT Cys	GGG Gly	GAC Asp	AAC Asn	GTG Val	CAG Gln	TTT Phe	GCC Ala	CCA Pro	CGC Arg	CAG Gln	CTG Leu	GGC Gly	CTG Leu	ACG Thr	1200
GAG Glu	CCT Pro	CGC Arg	ATC Ile	TAC Tyr	ATC Ile	AGC Ser	GAC Asp	CTG Leu	CTG Leu	GCC Ala	CAC His	ACG Thr	CAG Gln	TAC Tyr	ACC Thr	1248
TTT Phe	GAG Glu	ATC Ile	CAG Gln	GCT Ala	GTG Val	AAT Asn	GGG Gly	GTC Val	ACC Thr	GAC Asp	CAG Gln	AGC Ser	CCC Pro	TTC Phe	TCC Ser	1296
CCA 430	CAG Pro	TTT Phe	GCA Ala	TCA Ser	GTG Val	AAT Asn	ATC Ile	ACC Thr	ACC Thr	AAC Asn	CAG Gln	GCT Ala	GCT Ala	CCT Pro	TCA Ser	1344
GCC Ala	GTG Val	TCC Ser	ATA Ile	ATG Met	CAC His	CAG Gln	GTC Val	AGC Ser	CGC Arg	ACT Thr	GTG Val	GAC Asp	AGC Ser	ATT Ile	ACC Thr	1392
CTC Leu	TCG Ser	TGG Trp	TCT Ser	CAA Gln	CCT Pro	GAC Asp	CAG Gln	CCC Pro	AAT Asn	GGA Gly	GTC Val	ATC Ile	CTG Leu	GAT Asp	TAT Tyr	1440
GAG Glu	CTG Leu	CAA Gln	TAC Tyr	TAT Tyr	GAG Glu	AAG Lys	AAC Asn	CTG Leu	AGT Ser	GAG Glu	TTA Leu	AAT Asn	TCA Ser	ACA Thr	GCA Ala	1488
GTG Val	AAG Lys	AGC Ser	CCC Pro	ACC Thr	AAC Asn	ACT Thr	GTG Val	ACA Thr	GTG Val	CAA Gln	AAC Asn	CTC Leu	AAA Lys	GCT Ala	GGC Gly	1536
ACC 510	ATC Ile	TAT Tyr	GTC Val	TTC Phe	CAA Gln	GTG Val	CGA Arg	GCA Ala	CGT Arg	ACC Thr	GTG Val	GCT Ala	GGG Gly	TAT Tyr	GGC Gly	1584
CGG Arg	TAT Tyr	AGT Ser	GGC Gly	AAG Lys	ATG Met	TAC Tyr	TTC Phe	CAG Gln	ACC Thr	ATG Met	ACT Thr	GAA Glu	GCC Ala	GAG Glu	TAC Tyr	1632

CAG Gln	ACC Thr	AGT Ser	GTC Val 545	CAG Gln	GAG Glu	AAG Lys	CTG Leu	CCA Pro 550	CTC Leu	ATC Ile	ATT Ile	GGC Gly	TCC Ser 555	TCT Ser	GCA Ala	1680
GCA Ala	GGA Gly	CTG Leu 560	GTG Val	TTT Phe	CTC Leu	ATT Ile	GCT Ala 565	GTT Val	GTC Val	GTC Val	ATC Ile	ATT Ile 570	ATT Ile	GTC Val	TGC Cys	1728
AAC Asn	AGA Arg	AGA Arg	CGG Arg 575	GGC Gly	TTT Phe	GAA Ser 580	CGT Arg	GCT Ala	GAC Asp	TCT Ser	GAG Glu 585	TAC Tyr	ACT Thr	GAC Asp	AAG Lys	1776
CTG Leu 590	CAG Gln	CAC His	TAT Tyr	ACC Thr	AGT Ser 595	GGC Gly	CAC His	AGT Ser	ACG Thr	TAC Tyr 600	CGT Arg	GGT Gly	CCC Pro	CCG Pro	CCA Pro 605	1824
GGC Gly	CTG Leu	GGG Gly	GTC Val 610	CGC Arg	TCT Ser	CTC Leu	TTC Phe	GTG Val	ACT Thr 615	CCA Pro	GGG Gly	ATG Met	AAG Lys	ATT Ile 620	TAT Tyr	1872
ATC Ile	GAT Asp	CCA Pro	TTT Phe 625	ACC Thr	TAC Tyr	GAA Glu	GAT Asp	CCC Pro 630	AAT Asn	GAG Glu	GCT Ala	GTC Val	AGG Arg 635	GAA Glu	TTT Phe	1920
GCA Ala	AAA Lys	GAA Glu 640	ATT Ile	GAT Asp	ATC Ile	TCC Ser	TGT Cys 645	GTG Val	AAA Lys	ATC Ile	GAG Glu	CAG Gln 650	GTG Val	ATT Ile	GGG Gly	1968
GCA Ala	GGG Gly 655	GAG Glu	TTT Phe	GGT Gly	GAG Glu 660	GTG Val	TGC Cys	AGT Ser	GGG Gly	CAT His	CTC Leu 665	AAG Lys	CTT Leu	CCT Pro	GGC Gly	2016
AAA Lys 670	AGA Arg	GAG Glu	ATC Ile	TTT Phe 675	GTG Val	GCC Ala	ATC Ile	AAG Lys	ACC Thr 680	CTG Leu	AAG Lys	TCT Ser	GGT Gly	TAC Tyr 685	ACA Thr 685	2064
GAG Glu	AAG Lys	CAG Gln	AGA Arg 690	CGG Arg	GAC Asp	TTC Phe	CTG Leu	AGT Ser	GAA Glu 695	GCC Ala	AGC Ser	ATC Ile	ATG Met	GGG Gly 700	CAG Gln	2112
TTT Phe	GAC Asp	CAC His	CCC Pro 705	AAT Asn	GTC Val	ATC Ile	CAC His	CTG Leu 710	GAA Glu	GGG Gly	GTG Val	GTG Val	ACC Thr 715	AAG Lys	AGT Ser	2160
TCC Ser	CCA Pro	GTC Val 720	ATG Met	ATC Ile	ATT Ile	ACA Thr	GAG Glu 725	TTC Phe	ATG Met	GAG Glu	AAT Asn	GGC Gly 730	TCG Ser	TTG Leu	GAC Asp	2208
TCC Ser	TTC Phe 735	TTG Leu	AGG Arg	CAA Gln	AAT Asn	GAT Asp 740	GGG Gly	CAG Gln	TTC Phe	ACA Thr	GTG Val 745	ATC Ile	CAG Gln	CTG Leu	GTG Val	2256
GGC Gly 750	ATG Met	TTG Leu	CGT Arg	GGC Gly	ATT Ile 755	GCA Ala	GCA Ala	GGC Gly	ATG Met	AAG Lys 760	TAC Tyr	CTG Leu	GCT Ala	GAT Asp	ATG Met 765	2304
AAC Asn	TAC Tyr	GTG Val	CAC His 770	CGG Arg	GAC Asp	CTG Leu	GCT Ala	GCC Ala	CGC Arg 775	AAC Asn	ATC Ile	CTG Leu	GTC Val	AAC Asn 780	AGC Ser	2352
AAC Asn	CTG Leu	GTC Val	TGC Cys 785	AAG Lys	GTG Val	TCC Ser	GAC Asp 790	TTC Phe	GGC Gly	CTC Leu	TCC Ser	CGT Arg 795	TTC Phe	CTG Leu	GAG Glu	2400
GAT Asp	GAC Asp	ACC Thr 800	TCT Ser	GAT Asp	CCC Pro	ACT Thr	TAC Tyr 805	ACC Thr	AGC Ser	GCA Ala	CTG Leu	GGT Gly 810	GGA Gly	AAG Lys	ATC Ile	2448

CCA ATA CGG TGG ACA GCG CCT GAG GCA ATT CAG TAC CGA AAA TTC ACA	2496
Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Gln Tyr Arg Lys Phe Thr	
815 820 825	
TCA GCC AGC GAT GTG TGG AGC TAT GGA ATA GTC ATG TGG GAG GTG ATG	2544
Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met	
830 835 840 845	
TCG TAC GGC GAG CGG CCT TAC TGG GAC ATG ACC AAT CAA GAT GTG ATA	2592
Ser Tyr Gly Glu Arg Pro Tyr Trp Asp Met Thr Asn Gln Asp Val Ile	
850 855 860	
AAT GCT ATT GAG CAG GAC TAT CGG CTA CCA CCC CCT ATG GAT TGT CCA	2640
Asn Ala Ile Glu Gln Asp Tyr Arg Leu Pro Pro Pro Met Asp Cys Pro	
865 870 875	
AAT GCC CTG CAC CAG CTA ATG CTT GAC TGC TGG CAG AAG GAT CGA AAC	2688
Asn Ala Leu His Gln Leu Met Leu Asp Cys Trp Gln Lys Asp Arg Asn	
880 885 890	
CAC AGA CCC AAA TTT GGA CAG ATT GTC AAC ACT TTA GAC AAA ATG ATC	2736
His Arg Pro Lys Phe Gly Gln Ile Val Asn Thr Leu Asp Lys Met Ile	
895 900 905	
CGA AAT CCT AAT AGT CTG AAA GCC ATG GCA CCT CTC TCC TCT GGG GTT	2784
Arg Asn Pro Asn Ser Leu Lys Ala Met Ala Pro Leu Ser Ser Gly Val	
910 915 920 925	
AAC CTC CCT CTA CTT GAC CGC ACA ATC CCA GAT TAT ACC AGC TTC AAC	2832
Asn Leu Pro Leu Leu Asp Arg Thr Ile Pro Asp Tyr Thr Ser Phe Asn	
930 935 940	
ACT GTG GAT GAA TGG CTG GAT GCC ATC AAG ATG AGC CAG TAC AAG GAG	2880
Thr Val Asp Glu Trp Leu Asp Ala Ile Lys Met Ser Gln Tyr Lys Glu	
945 950 955	
AGC TTT GCC AGT GCT GGC TTC ACC ACC TTT GAT ATA GTA TCT CAG ATG	2928
Ser Phe Ala Ser Ala Gly Phe Thr Thr Phe Asp Ile Val Ser Gln Met	
960 965 970	
ACT GTA GAG GAC ATT CTA CGA GTT GGG GTC ACT TTA GCA GGA CAC CAG	2976
Thr Val Glu Asp Ile Leu Arg Val Gly Val Thr Leu Ala Gly His Gln	
975 980 985	
AAG AAA ATT CTG AAC AGT ATC CAG GTG ATG AGA GCA CAG ATG AAC CAA	3024
Lys Lys Ile Leu Asn Ser Ile Gln Val Met Arg Ala Gln Met Asn Gln	
990 995 1000 1005	
ATT CAG TCT GTG GAG GTT TGATAGCAAC ACGTCCTCGT GCTCCACTTC	3072
Ile Gln Ser Val Glu Val	
1010	
CTTGAGGCCC TGCTCCCCCTC TGCCCCCTGTG TGTCTGAGCT CCAGTTCTTG AGTGTCTGCTGC	3132
GTGGATCAGA GACAGGCAGC TGCTCTGAGG ATCATGGCAA CAGGAAGAAA TGCCCTATCA	3192
TTGACAACGA GAAGTCATCA AGAGGTGAAA CAATGGAAAA CAATGGAAAA AGGGAACAAG	3252
TAAAGACAGC TATTTTGA AAA ACCGAAAACA AACAGTGAAT TATTTTAAAA TAATAATAAA	3312
GCAATTGCAG TCTTGAAAAG GGCTCCAAGA CCAATGGGAG TCTCCAAAAGG AAGAGAATAG	3372
AGCAGCTTCA TCTATTTCCCT CTTACACAAG GGTTGCTGCA GCTGGGCCCA GACACTTCTG	3432
GAGTAACGAG ACTTTTCAAG AAGATGAATG CAAAGAATGG TCACAAGAAG CACTTCTCTT	3492
TCTCACATGG GATGGCAGCT CTGGGAATGC CCGGCAGTCC TTCCTGAAAAG CCCTGTTGGC	3552

75

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AAATCGAAGA GGAGAGCCGA AGCTCTTTGG TGCTGTGGAA CCAAGTGCAT CTCAGAAATT 3612
GTTGGACTTC TACAAAAGCT GAAGACATTC TTTTTTTTAA AACAAGTAAA CTGATACTAG 3672
AAGAGGCTGT TTCCGTCAAA TGAGAAGGAA TCTGTAACAC TGGCCCCGGG GGGGTGGGGA 3732
ATGGGGGAAA TCAGTCCTTT TTACATCTCT TTATTTTCTC TTGTCATGGA ACAGTTTTGT 3792
GAGTGACAGT TTCCTAAGGG TCCGTCCATC CACCCTCCAA TGGCATCATT GTTTCATACA 3852
TATCATATGC ACAAGACTTA TAGTGATGTC CTCACTCGAT GCCAATGATC TTTCCCCAGA 3912
AGACTTCCCA AGTACAGTAT GTAGTAGATT TTGATTACAA ATGCTGACGT GTACCTTTAT 3972
TTTTCGGTTG TCGTTGTTGG GAGATTCGTC CTTTACCTT GCTTTGTTAA CACCAATTTG 4032
TGAGTTTGGG GTTGAATTT TTTTGGTCTG TTGGGGTTGT TTTTTTTTTT TTTTTTTTTT 4092
AACCG 4097

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## (2) INFORMATION FOR SEQ ID NO:12:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1011 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: protein

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

```

Met Pro Gly Pro Glu Arg Thr Met Gly Pro Leu Trp Phe Cys Cys Leu
 1           5           10
Pro Leu Ala Leu Leu Pro Leu Leu Ala Ala Val Glu Glu Thr Leu Met
          20           25           30
Asp Ser Thr Thr Ala Thr Ala Glu Leu Gly Trp Met Val His Pro Pro
          35           40           45
Ser Gly Trp Glu Glu Val Ser Gly Tyr Asp Glu Asn Met Asn Thr Ile
 50           55           60
Arg Thr Tyr Gln Val Cys Asn Val Phe Glu Ser Ser Gln Asn Asn Trp
 65           70           75           80
Leu Arg Thr Lys Tyr Ile Arg Arg Arg Gly Ala His Arg Ile His Val
          85           90           95
Glu Met Lys Phe Ser Val Arg Asp Cys Ser Ser Ile Pro Asn Val Pro
          100          105          110
Gly Ser Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Tyr Glu Ser Asp Phe
          115          120          125
Asp Ser Ala Thr Lys Thr Phe Pro Asn Trp Met Glu Asn Pro Trp Met
          130          135          140
Lys Val Asp Thr Ile Ala Ala Asp Glu Ser Phe Ser Gln Val Asp Leu
          145          150          155          160
Gly Gly Arg Val Met Lys Ile Asn Thr Glu Val Arg Ser Phe Gly Pro
          165          170          175
Val Ser Lys Asn Gly Phe Tyr Leu Ala Phe Gln Asp Tyr Gly Gly Cys
          180          185          190

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Met Ser Leu Ile Ala Val Arg Val Phe Tyr Arg Lys Cys Pro Arg Val  
 195 200 205  
 Ile Gln Asn Gly Ala Val Phe Gln Glu Thr Leu Ser Gly Ala Glu Ser  
 210 215 220  
 Thr Ser Leu Val Ala Ala Arg Gly Thr Cys Ile Ser Asn Ala Glu Glu  
 225 230 235 240  
 Val Asp Val Pro Ile Lys Leu Tyr Cys Asn Gly Asp Gly Glu Trp Leu  
 245 250 255  
 Val Pro Ile Gly Arg Cys Met Cys Arg Pro Gly Tyr Glu Ser Val Glu  
 260 265 270  
 Asn Gly Thr Val Cys Arg Gly Cys Pro Ser Gly Thr Phe Lys Ala Ser  
 275 280 285  
 Gln Gly Asp Glu Gly Cys Val His Cys Pro Ile Asn Ser Arg Thr Thr  
 290 295 300  
 Ser Glu Gly Ala Thr Asn Cys Val Cys Arg Asn Gly Tyr Tyr Arg Ala  
 305 310 315 320  
 Asp Ala Asp Pro Val Asp Met Pro Cys Thr Thr Ile Pro Ser Ala Pro  
 325 330 335  
 Gln Ala Val Ile Ser Ser Val Asn Glu Thr Ser Leu Met Leu Glu Trp  
 340 345 350  
 Thr Pro Pro Arg Asp Ser Gly Gly Arg Glu Asp Leu Val Tyr Asn Ile  
 355 360 365  
 Ile Cys Lys Ser Cys Gly Ser Gly Arg Gly Ala Cys Thr Arg Cys Gly  
 370 375 380  
 Asp Asn Val Gln Phe Ala Pro Arg Gln Leu Gly Leu Thr Glu Pro Arg  
 385 390 395 400  
 Ile Tyr Ile Ser Asp Leu Leu Ala His Thr Gln Tyr Thr Phe Glu Ile  
 405 410 415  
 Gln Ala Val Asn Gly Val Thr Asp Gln Ser Pro Phe Ser Pro Gln Phe  
 420 425 430  
 Ala Ser Val Asn Ile Thr Thr Asn Gln Ala Ala Pro Ser Ala Val Ser  
 435 440 445  
 Ile Met His Gln Val Ser Arg Thr Val Asp Ser Ile Thr Leu Ser Trp  
 450 455 460  
 Ser Gln Pro Asp Gln Pro Asn Gly Val Ile Leu Asp Tyr Glu Leu Gln  
 465 470 475 480  
 Tyr Tyr Glu Lys Asn Leu Ser Glu Leu Asn Ser Thr Ala Val Lys Ser  
 485 490 495  
 Pro Thr Asn Thr Val Thr Val Gln Asn Leu Lys Ala Gly Thr Ile Tyr  
 500 505 510  
 Val Phe Gln Val Arg Ala Arg Thr Val Ala Gly Tyr Gly Arg Tyr Ser  
 515 520 525  
 Gly Lys Met Tyr Phe Gln Thr Met Thr Glu Ala Glu Tyr Gln Thr Ser  
 530 535 540

Val Gln Glu Lys Leu Pro Leu Ile Ile Gly Ser Ser Ala Ala Gly Leu  
 545 550 555 560  
 Val Phe Leu Ile Ala Val Val Val Ile Ile Ile Val Cys Asn Arg Arg  
 565 570 575  
 Arg Gly Phe Glu Arg Ala Asp Ser Glu Tyr Thr Asp Lys Leu Gln His  
 580 585 590  
 Tyr Thr Ser Gly His Ser Thr Tyr Arg Gly Pro Pro Pro Gly Leu Gly  
 595 600 605  
 Val Arg Ser Leu Phe Val Thr Pro Gly Met Lys Ile Tyr Ile Asp Pro  
 610 615 620  
 Phe Thr Tyr Glu Asp Pro Asn Glu Ala Val Arg Glu Phe Ala Lys Glu  
 625 630 635 640  
 Ile Asp Ile Ser Cys Val Lys Ile Glu Gln Val Ile Gly Ala Gly Glu  
 645 650 655  
 Phe Gly Glu Val Cys Ser Gly His Leu Lys Leu Pro Gly Lys Arg Glu  
 660 665 670  
 Ile Phe Val Ala Ile Lys Thr Leu Lys Ser Gly Tyr Thr Glu Lys Gln  
 675 680 685  
 Arg Arg Asp Phe Leu Ser Glu Ala Ser Ile Met Gly Gln Phe Asp His  
 690 695 700  
 Pro Asn Val Ile His Leu Glu Gly Val Val Thr Lys Ser Ser Pro Val  
 705 710 715 720  
 Met Ile Ile Thr Glu Phe Met Glu Asn Gly Ser Leu Asp Ser Phe Leu  
 725 730 735  
 Arg Gln Asn Asp Gly Gln Phe Thr Val Ile Gln Leu Val Gly Met Leu  
 740 745 750  
 Arg Gly Ile Ala Ala Gly Met Lys Tyr Leu Ala Asp Met Asn Tyr Val  
 755 760 765  
 His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser Asn Leu Val  
 770 775 780  
 Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Phe Leu Glu Asp Asp Thr  
 785 790 795 800  
 Ser Asp Pro Thr Tyr Thr Ser Ala Leu Gly Gly Lys Ile Pro Ile Arg  
 805 810 815  
 Trp Thr Ala Pro Glu Ala Ile Gln Tyr Arg Lys Phe Thr Ser Ala Ser  
 820 825 830  
 Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met Ser Tyr Gly  
 835 840 845  
 Glu Arg Pro Tyr Trp Asp Met Thr Asn Gln Asp Val Ile Asn Ala Ile  
 850 855 860  
 Glu Gln Asp Tyr Arg Leu Pro Pro Pro Met Asp Cys Pro Asn Ala Leu  
 865 870 875 880  
 His Gln Leu Met Leu Asp Cys Trp Gln Lys Asp Arg Asn His Arg Pro  
 885 890 895

[illegible]

(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 3591 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: both  
(D) TOPOLOGY: linear

(ix) **FEATURE:**

- (A) NAME/KEY: CDS  
(B) LOCATION: 2..2965

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

C	GGG	GTC	TCC	TCG	AGG	GCG	CGG	CGG	CCG	CCG	GGC	AGC	AGC	AGG	AGC	46
Gly	Val	Ser	Ser	Ser	Arg	Ala	Arg	Arg	Pro	Pro	Gly	Ser	Ser	Arg	Ser	
1					5					10					15	
AGC	AGG	AGG	GGG	GTG	ACC	TCG	GAG	CTG	GCA	TGG	ACA	ACC	CAT	CCG	GAG	94
Ser	Arg	Arg	Gly	Val	Thr	Ser	Glu	Leu	Ala	Trp	Thr	Thr	His	Pro	Glu	
				20					25					30		
ACG	GGG	TGG	GAA	GAG	GTC	AGT	GGT	TAC	GAC	GAG	GCT	ATG	AAC	CCC	ATC	142
Thr	Gly	Trp	Glu	Glu	Val	Ser	Gly	Tyr	Asp	Glu	Ala	Met	Asn	Pro	Ile	
			35					40					45			
CGC	ACA	TAC	CAG	GTG	TGC	AAC	GTG	CGG	GAG	GCC	AAC	CAG	AAC	AAC	TGG	190
Arg	Thr	Tyr	Gln	Val	Cys	Asn	Val	Arg	Glu	Ala	Asn	Gln	Asn	Asn	Trp	
		50					55					60				
CTT	CGC	ACC	AAG	TTC	ATT	CAG	CGC	CAG	GAC	GTC	CAG	CGT	GTC	TAC	GTG	238
Leu	Arg	Thr	Lys	Phe	Ile	Gln	Arg	Gln	Asp	Val	Gln	Arg	Val	Tyr	Val	
	65					70					75					
GAG	CTG	AAA	TTC	ACT	GTG	CGG	GAC	TGC	AAC	AGC	ATC	CCC	AAC	ATC	CCT	286
Glu	Leu	Lys	Phe	Thr	Val	Arg	Asp	Cys	Asn	Ser	Ile	Pro	Asn	Ile	Pro	
80					85					90					95	
GGT	TCC	TGC	AAA	GAG	ACC	TTC	AAC	CTC	TTC	TAT	TAT	GAG	TCA	GAT	ACG	334
Gly	Ser	Cys	Lys	Glu	Thr	Phe	Asn	Leu	Phe	Tyr	Tyr	Glu	Ser	Asp	Thr	
				100					105					110		



GAT	TCT	GCC	TCT	GCC	AAT	AGC	CCT	TTC	TGG	ATG	GAG	AAC	CCC	TAT	ATC	382
Asp	Ser	Ala	Ser	Ala	Asn	Ser	Pro	Phe	Trp	Met	Glu	Asn	Pro	Tyr	Ile	
			115					120					125			
AAA	GTG	GAT	ACA	ATT	GCT	CCG	GAT	GAG	AGC	TTC	TCC	AAA	CTG	GAG	TCC	430
Lys	Val	Asp	Thr	Ile	Ala	Pro	Asp	Glu	Ser	Phe	Ser	Lys	Leu	Glu	Ser	
			130					135					140			
GGC	CGT	GTG	AAC	ACC	AAG	GTG	CGC	AGC	TTT	GGG	CCG	CTC	TCC	AAG	AAT	478
Gly	Arg	Val	Asn	Thr	Lys	Val	Arg	Ser	Phe	Gly	Pro	Leu	Ser	Lys	Asn	
			145					150					155			
GGC	TTT	TAT	CTG	GCT	TTC	CAG	GAC	CTG	GGG	GCC	TGC	ATG	TCC	CTT	ATC	526
Gly	Phe	Tyr	Leu	Ala	Phe	Gln	Asp	Leu	Gly	Ala	Cys	Met	Ser	Leu	Ile	
					165					170					175	
TCC	GTC	CGG	GCT	TTC	TAC	AAG	AAA	TGT	TCC	AAC	ACC	ATC	GCT	GGC	TTT	574
Ser	Val	Arg	Ala	Phe	Tyr	Lys	Lys	Cys	Ser	Asn	Thr	Ile	Ala	Gly	Phe	
					180					185					190	
GCT	ATC	TTC	CCG	GAG	ACC	CTA	ACG	GGG	GCT	GAG	CCC	ACG	TCG	CTG	GTC	622
Ala	Ile	Phe	Pro	Glu	Thr	Leu	Thr	Gly	Ala	Glu	Pro	Thr	Ser	Leu	Val	
					195				200					205		
ATT	GCG	CCG	GGC	ACC	TGC	ATC	CCC	AAC	GCA	GTG	GAA	GTG	TCT	GTG	CCC	670
Ile	Ala	Pro	Gly	Thr	Cys	Ile	Pro	Asn	Ala	Val	Glu	Val	Ser	Val	Pro	
					210			215					220			
CTG	AAG	CTG	TAC	TGC	AAC	GGT	GAT	GGC	GAG	TGG	ATG	GTG	CCT	GTG	GGA	718
Leu	Lys	Leu	Tyr	Cys	Asn	Gly	Asp	Gly	Glu	Trp	Met	Val	Pro	Val	Gly	
						230						235				
GCG	TGC	ACG	TGT	GCT	GCT	GGG	TAC	GAG	CCA	GCC	ATG	AAG	GAT	ACC	CAG	766
Ala	Cys	Thr	Cys	Ala	Ala	Gly	Tyr	Glu	Pro	Ala	Met	Lys	Asp	Thr	Gln	
						245					250				255	
TGC	CAA	GCA	TGC	GGC	CCG	GGG	ACG	TTC	AAA	TCC	AAG	CAG	GGC	GAG	GGC	814
Cys	Gln	Ala	Cys	Gly	Pro	Gly	Thr	Phe	Lys	Ser	Lys	Gln	Gly	Glu	Gly	
						260				265					270	
CCC	TGC	TCC	CCC	TGC	CCT	CCC	AAC	AGC	CGC	ACC	ACC	GCG	GGG	GCA	GCC	862
Pro	Cys	Ser	Pro	Cys	Pro	Pro	Asn	Ser	Arg	Thr	Thr	Ala	Gly	Ala	Ala	
						275							285			
ACA	GTC	TGC	ATA	TGT	CGC	AGC	GGC	TTC	TTC	CGA	GCA	GAC	GCG	GAC	CCC	910
Thr	Val	Cys	Ile	Cys	Arg	Ser	Gly	Phe	Phe	Arg	Ala	Asp	Ala	Asp	Pro	
							295						300			
GCA	GAC	AGC	GCC	TGC	ACC	AGT	GTG	CCC	TCA	GCC	CCA	CGC	AGC	GTC	ATC	958
Ala	Asp	Ser	Ala	Cys	Thr	Ser	Val	Pro	Ser	Ala	Pro	Arg	Ser	Val	Ile	
						310						315				
TCC	AAC	GTG	AAT	GAG	ACG	TCG	TTG	GTG	CTG	GAG	TGG	AGC	GAG	CCG	CAG	1006
Ser	Asn	Val	Asn	Glu	Thr	Ser	Leu	Val	Leu	Glu	Trp	Ser	Glu	Pro	Gln	
							325								335	
GAC	GCG	GGC	GGG	CGG	GAT	GAC	CTG	CTC	TAC	AAC	GTC	ATC	TGC	AAG	AAG	1054
Asp	Ala	Gly	Gly	Arg	Asp	Asp	Leu	Leu	Tyr	Asn	Val	Ile	Cys	Lys	Lys	
							340								350	
TGC	AGC	GTG	GAG	CGG	CGG	CTG	TGC	AGC	CGC	TGC	GAC	GAC	AAC	GTG	GAG	1102
Cys	Ser	Val	Glu	Arg	Arg	Leu	Cys	Ser	Arg	Cys	Asp	Asp	Asn	Val	Glu	
								360						365		
TTC	GTG	CCG	CGC	CAG	CTG	GGC	CTC	ACT	GGC	CTC	ACT	GAG	CGA	CGC	ATC	1150
Phe	Val	Pro	Arg	Gln	Leu	Gly	Leu	Thr	Gly	Leu	Thr	Glu	Arg	Arg	Ile	
							375						380			

80

TAC Tyr 385	ATC Ile	AGC Ser	AAG Lys	GTG Val	ATG Met	GCC Ala 390	CAC His	CCC Pro	CAG Gln	TAC Tyr 395	ACC Thr 395	TTC Phe	GAG Glu	ATC Ile	CAG Gln	1198
GCG Ala 400	GTG Val	AAT Asn	GGC Gly	ATC Ile	TCC Ser 405	AGC Ser	AAG Lys	AGC Ser	CCC Pro	TAC Tyr 410	CCT Pro	CCC Pro	CAT His	TTT Phe	GCC Ala 415	1246
TCC Ser	GTC Val	AAC Asn	ATC Ile	ACG Thr 420	ACC Thr	AAC Asn	CAG Gln	GCA Ala	GCC Ala 425	CCA Pro	TCT Ser	GCC Ala	GTG Val	CCC Pro 430	ACC Thr	1294
ATG Met	CAT His	CTG Leu	CAC His 435	AGC Ser	AGC Ser	ACC Thr	GGG Gly 440	AAC Asn	AGC Ser	ATG Met	ACA Thr	CTG Leu	TCA Ser 445	TGG Trp	ACT Thr	1342
CCC Pro	CCG Pro	GAA Glu 450	AGG Arg	CCC Pro	AAC Asn	GGC Gly 455	ATC Ile 455	ATT Ile	CTC Leu	GAC Asp	TAT Tyr 460	GAA Glu 460	ATC Ile	AAG Lys	TAC Tyr	1390
TCC Ser	GAG Glu 465	AAG Lys	CAA Gln	GGC Gly	CAG Gln 470	GGT Gly	GAC Asp	GGC Gly	ATT Ile	GCC Ala	AAC Asn 475	ACT Thr	GTC Val	ACC Thr	AGC Ser	1438
CAG Gln 480	AAG Lys	AAC Asn	TCG Ser	GTG Val	CGG Arg 485	CTG Leu	GAC Asp	GGA Gly	CTG Leu	AAG Lys 490	GCC Ala	AAT Asn	GCT Ala	CGG Arg	TAC Tyr 495	1486
ATG Met	GTG Val	CAG Gln	GTC Val	CGG Arg 500	GCG Ala	CGC Arg	ACA Thr	GTG Val	GCT Ala 505	GGA Gly	TAC Tyr	GGC Gly	CGC Arg	TAC Tyr 510	AGC Ser	1534
CTC Leu	CCC Pro	ACC Thr	GAG Glu 515	TTC Phe	CAG Gln	ACG Thr	ACT Thr	GCG Ala 520	GAG Glu	GAT Asp	GGC Gly	TCC Ser	ACC Thr 525	AGC Ser	AAG Lys	1582
ACT Thr	TTC Phe	CAG Gln 530	GAG Glu	CTT Leu	CCT Pro	CTC Leu	ATC Ile 535	GTG Val	GGT Gly	TCA Ser	GCC Ala	ACC Thr 540	GCG Ala	GGA Gly	CTG Leu	1630
CTG Leu	TTT Phe 545	GTC Val	ATC Ile	GTG Val	GTG Val 550	GTC Val	ATC Ile	ATC Ile	GCT Ala	ATT Ile	GTC Val 555	TGC Cys	TTC Phe	AGG Arg	AAA Lys	1678
GGG Gly 560	ATG Met	GTT Val	ACT Thr	GAA Glu	CAA Gln 565	CTC Leu	CTC Leu	TCG Ser	TCT Ser	CCT Pro 570	TTG Leu	GGC Gly	AGG Arg	AAG Lys	CAG Gln 575	1726
CGC Arg	AAC Asn	AGC Ser	ACA Thr	GAT Asp 580	CCC Pro	GAG Glu	TAC Tyr	ACA Thr	GAG Glu 585	AAG Lys	CTG Leu	CAG Gln	CAA Gln	TAT Tyr 590	GTC Val	1774
ACT Thr	CCT Pro	GGG Gly 595	ATG Met	AAG Lys	GTC Val	TAC Tyr	ATT Ile	GAC Asp 600	CCC Pro	TTC Phe	ACC Thr	TAT Tyr 605	GAA Glu	GAC Asp	CCA Pro	1822
AAT Asn	GAA Glu	GCT Ala 610	GTC Val	CGG Arg	GAA Glu	TTC Phe	GCC Ala 615	AAA Lys	GAG Glu	ATT Ile	GAT Asp 620	ATC Ile	TCC Ser	TGT Cys	GTC Val	1870
AAA Lys	ATT Ile 625	GAG Glu	GAG Glu	GTC Val	ATT Ile	GGA Gly 630	GCA Ala	GGA Gly	GAG Glu	TTT Phe	GGT Gly 635	GAG Glu	GTG Val	TGC Cys	CGT Arg	1918
GGG Gly 640	CGC Arg	CTG Leu	AAG Lys	CTG Leu	CCT Pro 645	GGC Gly	CGC Arg	CGT Arg	GAG Glu	ATC Ile 650	TTT Phe	GTG Val	GCC Ala	ATC Ile	AAG Lys 655	1966

81

ACA	CTG	AAG	GTG	GGC	TAC	ACA	GAG	AGG	CAG	CGG	CGG	GAC	TTC	CTG	AGT	2014
Thr	Leu	Lys	Val	Gly	Tyr	Thr	Glu	Arg	Gln	Arg	Arg	Asp	Phe	Leu	Ser	
				660					665					670		
GAG	GCC	AGC	ATC	ATG	GGC	CAG	TTC	GAC	CAC	CCC	AAC	ATC	ATC	CAC	CTG	2062
Glu	Ala	Ser	Ile	Met	Gly	Gln	Phe	Asp	His	Pro	Asn	Ile	Ile	His	Leu	
			675					680					685			
GAG	GGC	GTG	GTG	ACC	AAG	AGC	CGC	CCT	GTC	ATG	ATC	ATC	ACA	GAG	TTC	2110
Glu	Gly	Val	Val	Thr	Lys	Ser	Arg	Pro	Val	Met	Ile	Ile	Thr	Glu	Phe	
		690					695					700				
ATG	GAG	AAC	TGC	GCT	CTC	GAC	TCC	TTC	CTC	CGG	CTG	AAT	GAT	GGG	CAG	2158
Met	Glu	Asn	Cys	Ala	Leu	Asp	Ser	Phe	Leu	Arg	Leu	Asn	Asp	Gly	Gln	
	705					710					715					
TTC	ACG	GTC	ATC	CAG	CTG	GTG	GGG	ATG	CTG	CGA	GGC	ATC	GCT	GCT	GGC	2206
Phe	Thr	Val	Ile	Gln	Leu	Val	Gly	Met	Leu	Arg	Gly	Ile	Ala	Ala	Gly	
720					725					730					735	
ATG	AAG	TAC	CTC	TCA	GAG	ATG	AAC	TAC	GTG	CAC	CGA	GAC	CTG	GCT	GCC	2254
Met	Lys	Tyr	Leu	Ser	Glu	Met	Asn	Tyr	Val	His	Arg	Asp	Leu	Ala	Ala	
				740					745					750		
CGC	AAC	ATC	CTG	GTC	AAC	AGC	AAC	TTG	GTC	TGC	AAA	GTG	TCT	GAC	TTC	2302
Arg	Asn	Ile	Leu	Val	Asn	Ser	Asn	Leu	Val	Cys	Lys	Val	Ser	Asp	Phe	
			755					760					765			
GGG	CTC	TCC	CGC	TTT	TTG	GAG	GAT	GAT	CCA	GCC	GAC	CCC	ACC	TAC	ACC	2350
Gly	Leu	Ser	Arg	Phe	Leu	Glu	Asp	Asp	Pro	Ala	Asp	Pro	Thr	Tyr	Thr	
		770					775					780				
AGC	TCC	CTG	GGA	GGC	AAG	ATC	CCC	ATC	AGG	TGG	ACA	GCT	CCT	GAG	GCC	2398
Ser	Ser	Leu	Gly	Gly	Lys	Ile	Pro	Ile	Arg	Trp	Thr	Ala	Pro	Glu	Ala	
	785					790					795					
ATC	GCC	TAC	CGC	AAA	TTC	ACG	TCG	GCC	AGC	GAC	GTG	TGG	AGC	TAC	GGC	2446
Ile	Ala	Tyr	Arg	Lys	Phe	Thr	Ser	Ala	Ser	Asp	Val	Trp	Ser	Tyr	Gly	
800					805					810					815	
ATC	GTC	ATG	TGG	GAA	GTG	ATG	TCC	TAC	GGG	GAG	CGA	CCC	TAC	TGG	GAC	2494
Ile	Val	Met	Trp	Glu	Val	Met	Ser	Tyr	Gly	Glu	Arg	Pro	Tyr	Trp	Asp	
				820					825					830		
ATG	TCC	AAC	CAG	GAT	GTG	ATC	AAC	GCG	GTG	GAG	CAG	GAT	TAC	CGC	CTG	2542
Met	Ser	Asn	Gln	Asp	Val	Ile	Asn	Ala	Val	Glu	Gln	Asp	Tyr	Arg	Leu	
			835					840					845			
CCA	CCC	CCC	ATG	GAC	TGC	CCC	ACA	GCA	CTG	CAC	CAG	CTG	ATG	CTG	GAC	2590
Pro	Pro	Pro	Met	Asp	Cys	Pro	Thr	Ala	Leu	His	Gln	Leu	Met	Leu	Asp	
		850					855					860				
TGC	TGG	GTG	CGG	GAC	CGC	AAC	CTG	CGG	CCC	AAG	TTT	GCA	CAG	ATT	GTC	2638
Cys	Trp	Val	Arg	Asp	Arg	Asn	Leu	Arg	Pro	Lys	Phe	Ala	Gln	Ile	Val	
	865					870					875					
AAC	ACG	CTG	GAC	AAG	CTG	ATC	CGC	AAT	GCT	GCC	AGC	CTG	AAG	GTC	ATC	2686
Asn	Thr	Leu	Asp	Lys	Leu	Ile	Arg	Asn	Ala	Ala	Ser	Leu	Lys	Val	Ile	
880					885					890					895	
GCC	AGC	GTC	CAG	TCC	GGT	GTC	TCC	CAG	CCG	CTC	CTG	GAC	CGC	ACC	GTG	2734
Ala	Ser	Val	Gln	Ser	Gly	Val	Ser	Gln	Pro	Leu	Leu	Asp	Arg	Thr	Val	
				900					905					910		
CCC	GAT	TAC	ACC	ACC	TTC	ACC	ACC	GTG	GGA	GAC	TGG	CTG	GAT	GCC	ATC	2782
Pro	Asp	Tyr	Thr	Thr	Phe	Thr	Thr	Val	Gly	Asp	Trp	Leu	Asp	Ala	Ile	
			915					920					925			

82

AAA ATG GGA CGG TAC AAG GAG AAC TTC GTC AAC GCC GGC TTC GCC TCC	2830
Lys Met Gly Arg Tyr Lys Glu Asn Phe Val Asn Ala Gly Phe Ala Ser	
930 935 940	
TTT GAC CTG GTG GCA CAG ATG ACA GCA GAG GAC CTG CTA AGG ATA GGA	2878
Phe Asp Leu Val Ala Gln Met Thr Ala Glu Asp Leu Leu Arg Ile Gly	
945 950 955	
GTG ACG CTA GCA GGG CAC CAG AAG AAG ATC CTG AGC AGC ATT CAG GAC	2926
Val Thr Leu Ala Gly His Gln Lys Lys Ile Leu Ser Ser Ile Gln Asp	
960 965 970 975	
ATG AGG CTG CAG ATG AAC CAG ACG CTG CCG GTT CAG GTT TGACCGCAGG	2975
Met Arg Leu Gln Met Asn Gln Thr Leu Pro Val Gln Val	
980 985	
GACTCTGCAT TGGAACGGAC TGAGGGAACC TGCCAACCAG GTTCTGTTTG CGGTGCAGCC	3035
CGGCTTCCCG ATTTCCCCTT CCCGTGGCGC TCCTCTGCCT CGGACGCTCG CCGGGGACAG	3095
GCTGGGCCGG GCCACCCTTC CCTGGATCAG AGGCACTCGT GCCGGGAGGG AGCCCGGCTT	3155
TTCGTCCCGT GTCCCGCAGC GGCGAGGCAG TGAACGCAGT CTTCATATTG AAGATGGATT	3215
ATGGGACGGA GATGGCGCAT CCGCTTCCCG CCCTGTCTCA GTGCTCATCA GTTTGAAGAG	3275
ATGTTCTGCT TCTTGGATTT CTTTACACCC CGGTTTTCCC CCCTCGAGTC CTCACTTCCC	3335
CCTATCCCTG AGGCCACAGA CTGTTGACCC GTCCGCTGAG TCCGTCAGAC GCTCCGAAGC	3395
CTTCCCCGAG CCCGGTCCCC GCGTGGAGAC GGCGCCAGGG ACGGGGCTAC GGCCCCAGAC	3455
AATCACTCCA CCCCTCCGCA CGAGGGTCCT CACTGGGACG TGTCTGAAGG GGAAAGGCTC	3515
TGCTCCCTTT TTGGCTTTGC ACGCCAGAAC CCGAACCCCG TGAGATTTAC TATGCAGGGA	3575
GTTAGGCAAA AAAAAG	3591

## (2) INFORMATION FOR SEQ ID NO:14:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 988 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: protein

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

Gly Val Ser Ser Arg Ala Arg Arg Pro Pro Gly Ser Ser Arg Ser Ser	
1 5 10 15	
Arg Arg Gly Val Thr Ser Glu Leu Ala Trp Thr Thr His Pro Glu Thr	
20 25 30	
Gly Trp Glu Glu Val Ser Gly Tyr Asp Glu Ala Met Asn Pro Ile Arg	
35 40 45	
Thr Tyr Gln Val Cys Asn Val Arg Glu Ala Asn Gln Asn Asn Trp Leu	
50 55 60	
Arg Thr Lys Phe Ile Gln Arg Gln Asp Val Gln Arg Val Tyr Val Glu	
65 70 75 80	
Leu Lys Phe Thr Val Arg Asp Cys Asn Ser Ile Pro Asn Ile Pro Gly	
85 90 95	

Ser Cys Lys Glu Thr Phe Asn Leu Phe Tyr Tyr Glu Ser Asp Thr Asp  
 100 105 110  
 Ser Ala Ser Ala Asn Ser Pro Phe Trp Met Glu Asn Pro Tyr Ile Lys  
 115 120 125  
 Val Asp Thr Ile Ala Pro Asp Glu Ser Phe Ser Lys Leu Glu Ser Gly  
 130 135 140  
 Arg Val Asn Thr Lys Val Arg Ser Phe Gly Pro Leu Ser Lys Asn Gly  
 145 150 155 160  
 Phe Tyr Leu Ala Phe Gln Asp Leu Gly Ala Cys Met Ser Leu Ile Ser  
 165 170 175  
 Val Arg Ala Phe Tyr Lys Lys Cys Ser Asn Thr Ile Ala Gly Phe Ala  
 180 185 190  
 Ile Phe Pro Glu Thr Leu Thr Gly Ala Glu Pro Thr Ser Leu Val Ile  
 195 200 205  
 Ala Pro Gly Thr Cys Ile Pro Asn Ala Val Glu Val Ser Val Pro Leu  
 210 215 220  
 Lys Leu Tyr Cys Asn Gly Asp Gly Glu Trp Met Val Pro Val Gly Ala  
 225 230 235 240  
 Cys Thr Cys Ala Ala Gly Tyr Glu Pro Ala Met Lys Asp Thr Gln Cys  
 245 250 255  
 Gln Ala Cys Gly Pro Gly Thr Phe Lys Ser Lys Gln Gly Glu Gly Pro  
 260 265 270  
 Cys Ser Pro Cys Pro Pro Asn Ser Arg Thr Thr Ala Gly Ala Ala Thr  
 275 280 285  
 Val Cys Ile Cys Arg Ser Gly Phe Phe Arg Ala Asp Ala Asp Pro Ala  
 290 295 300  
 Asp Ser Ala Cys Thr Ser Val Pro Ser Ala Pro Arg Ser Val Ile Ser  
 305 310 315 320  
 Asn Val Asn Glu Thr Ser Leu Val Leu Glu Trp Ser Glu Pro Gln Asp  
 325 330 335  
 Ala Gly Gly Arg Asp Asp Leu Leu Tyr Asn Val Ile Cys Lys Lys Cys  
 340 345 350  
 Ser Val Glu Arg Arg Leu Cys Ser Arg Cys Asp Asp Asn Val Glu Phe  
 355 360 365  
 Val Pro Arg Gln Leu Gly Leu Thr Gly Leu Thr Glu Arg Arg Ile Tyr  
 370 375 380  
 Ile Ser Lys Val Met Ala His Pro Gln Tyr Thr Phe Glu Ile Gln Ala  
 385 390 395 400  
 Val Asn Gly Ile Ser Ser Lys Ser Pro Tyr Pro Pro His Phe Ala Ser  
 405 410 415  
 Val Asn Ile Thr Thr Asn Gln Ala Ala Pro Ser Ala Val Pro Thr Met  
 420 425 430  
 His Leu His Ser Ser Thr Gly Asn Ser Met Thr Leu Ser Trp Thr Pro  
 435 440 445

84

Pro Glu Arg Pro Asn Gly Ile Ile Leu Asp Tyr Glu Ile Lys Tyr Ser  
 450 455 460  
 Glu Lys Gln Gly Gln Gly Asp Gly Ile Ala Asn Thr Val Thr Ser Gln  
 465 470 475 480  
 Lys Asn Ser Val Arg Leu Asp Gly Leu Lys Ala Asn Ala Arg Tyr Met  
 485 490 495  
 Val Gln Val Arg Ala Arg Thr Val Ala Gly Tyr Gly Arg Tyr Ser Leu  
 500 505 510  
 Pro Thr Glu Phe Gln Thr Thr Ala Glu Asp Gly Ser Thr Ser Lys Thr  
 515 520 525  
 Phe Gln Glu Leu Pro Leu Ile Val Gly Ser Ala Thr Ala Gly Leu Leu  
 530 535 540  
 Phe Val Ile Val Val Val Ile Ile Ala Ile Val Cys Phe Arg Lys Gly  
 545 550 555 560  
 Met Val Thr Glu Gln Leu Leu Ser Ser Pro Leu Gly Arg Lys Gln Arg  
 565 570 575  
 Asn Ser Thr Asp Pro Glu Tyr Thr Glu Lys Leu Gln Gln Tyr Val Thr  
 580 585 590  
 Pro Gly Met Lys Val Tyr Ile Asp Pro Phe Thr Tyr Glu Asp Pro Asn  
 595 600 605  
 Glu Ala Val Arg Glu Phe Ala Lys Glu Ile Asp Ile Ser Cys Val Lys  
 610 615 620  
 Ile Glu Glu Val Ile Gly Ala Gly Glu Phe Gly Glu Val Cys Arg Gly  
 625 630 635 640  
 Arg Leu Lys Leu Pro Gly Arg Arg Glu Ile Phe Val Ala Ile Lys Thr  
 645 650 655  
 Leu Lys Val Gly Tyr Thr Glu Arg Gln Arg Arg Asp Phe Leu Ser Glu  
 660 665 670  
 Ala Ser Ile Met Gly Gln Phe Asp His Pro Asn Ile Ile His Leu Glu  
 675 680 685  
 Gly Val Val Thr Lys Ser Arg Pro Val Met Ile Ile Thr Glu Phe Met  
 690 695 700  
 Glu Asn Cys Ala Leu Asp Ser Phe Leu Arg Leu Asn Asp Gly Gln Phe  
 705 710 715 720  
 Thr Val Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ala Gly Met  
 725 730 735  
 Lys Tyr Leu Ser Glu Met Asn Tyr Val His Arg Asp Leu Ala Ala Arg  
 740 745 750  
 Asn Ile Leu Val Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly  
 755 760 765  
 Leu Ser Arg Phe Leu Glu Asp Asp Pro Ala Asp Pro Thr Tyr Thr Ser  
 770 775 780  
 Ser Leu Gly Gly Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile  
 785 790 795 800

85

Ala	Tyr	Arg	Lys	Phe 805	Thr	Ser	Ala	Ser	Asp 810	Val	Trp	Ser	Tyr	Gly 815	Ile
Val	Met	Trp	Glu 820	Val	Met	Ser	Tyr	Gly 825	Glu	Arg	Pro	Tyr	Trp 830	Asp	Met
Ser	Asn	Gln	Asp 835	Val	Ile	Asn	Ala 840	Val	Glu	Gln	Asp	Tyr 845	Arg	Leu	Pro
Pro	Pro 850	Met	Asp	Cys	Pro	Thr 855	Ala	Leu	His	Gln	Leu 860	Met	Leu	Asp	Cys
Trp 865	Val	Arg	Asp	Arg	Asn 870	Leu	Arg	Pro	Lys	Phe 875	Ala	Gln	Ile	Val	Asn 880
Thr	Leu	Asp	Lys	Leu 885	Ile	Arg	Asn	Ala 890	Ala	Ser	Leu	Lys	Val	Ile 895	Ala
Ser	Val	Gln	Ser 900	Gly	Val	Ser	Gln	Pro 905	Leu	Leu	Asp	Arg	Thr 910	Val	Pro
Asp	Tyr	Thr 915	Thr	Phe	Thr	Thr	Val 920	Gly	Asp	Trp	Leu	Asp 925	Ala	Ile	Lys
Met	Gly 930	Arg	Tyr	Lys	Glu	Asn 935	Phe	Val	Asn	Ala	Gly 940	Phe	Ala	Ser	Phe
Asp 945	Leu	Val	Ala	Gln	Met 950	Thr	Ala	Glu	Asp	Leu 955	Leu	Arg	Ile	Gly	Val 960
Thr	Leu	Ala	Gly	His 965	Gln	Lys	Lys	Ile	Leu 970	Ser	Ser	Ile	Gln	Asp 975	Met
Arg	Leu	Gln	Met 980	Asn	Gln	Thr	Leu	Pro 985	Val	Gln	Val				

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 3254 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: both  
(D) TOPOLOGY: linear

(ix) **FEATURE:**

- (A) NAME/KEY: CDS  
(B) LOCATION: 32..2980

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

CGCTCTGCTC	GCGCGCTGCT	GCCCCGCCGA	C	ATG	GAC	CGC	CGC	CGC	CTG	CCG						52
				Met	Asp	Arg	Arg	Arg	Leu	Pro						
				1				5								
CTG	CTG	CTG	CTC	TGC	GCT	GCC	CTC	GGC	TCC	GCC	GGG	CGT	CTG	AGC	GCC	100
Leu	Leu	Leu	Leu	Cys	Ala	Ala	Leu	Gly	Ser	Ala	Gly	Arg	Leu	Ser	Ala	
		10					15					20				
CGC	CCC	GGC	AAC	GAA	GTT	AAT	CTG	CTG	GAT	TCA	AAA	ACA	ATT	CAA	GGG	148
Arg	Pro	Gly	Asn	Glu	Val	Asn	Leu	Leu	Asp	Ser	Lys	Thr	Ile	Gln	Gly	
	25					30					35					
GAG	CTG	GGC	TGG	ATC	TCC	TAC	CCA	TCA	CAT	GGG	TGG	GAA	GAG	ATT	AGT	196
Glu	Leu	Gly	Trp	Ile	Ser	Tyr	Pro	Ser	His	Gly	Trp	Glu	Glu	Ile	Ser	
40					45					50					55	

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GGT	GTT	GAT	GAG	CAT	TAT	ACT	CCA	ATC	AGA	ACT	TAC	CAA	GAG	AGC	AAT	244
Gly	Val	Asp	Glu	His	Tyr	Thr	Pro	Ile	Arg	Thr	Tyr	Gln	Glu	Ser	Asn	
				60					65					70		
GTT	ATG	GAT	CAC	AGT	CAA	AAC	AAT	TGG	CTG	CGA	ACA	AAC	TGG	ATT	CCA	292
Val	Met	Asp	His	Ser	Gln	Asn	Asn	Trp	Leu	Arg	Thr	Asn	Trp	Ile	Pro	
			75					80					85			
CGC	AAT	TCA	GCG	CAG	AAG	ATA	TAT	GTG	GAG	CTC	AAG	TTT	ACC	TTG	AGG	340
Arg	Asn	Ser	Ala	Gln	Lys	Ile	Tyr	Val	Glu	Leu	Lys	Phe	Thr	Leu	Arg	
		90					95					100				
GAC	TGC	AAT	AGT	ATC	CCT	CTA	GTT	CTG	GGC	ACT	TGC	AAA	GAG	ACT	TTC	388
Asp	Cys	Asn	Ser	Ile	Pro	Leu	Val	Leu	Gly	Thr	Cys	Lys	Glu	Thr	Phe	
	105					110					115					
AAT	CTG	TAT	TAC	ATG	GAA	TCC	GAT	GAT	GAC	CAT	TTG	GCA	AAG	TTC	AGA	436
Asn	Leu	Tyr	Tyr	Met	Glu	Ser	Asp	Asp	Asp	His	Leu	Ala	Lys	Phe	Arg	
	120				125					130					135	
GAG	CAC	CAA	TTT	ACG	AAG	ATT	GAC	ACC	ATG	GCG	GCT	GAT	GAG	AGC	TTC	484
Glu	His	Gln	Phe	Thr	Lys	Ile	Asp	Thr	Met	Ala	Ala	Asp	Glu	Ser	Phe	
				140					145					150		
ACC	CAG	ATG	GAT	CTT	GGG	GAC	CGG	ATT	CTC	AAG	CTG	AAT	ACC	GAA	GTC	532
Thr	Gln	Met	Asp	Leu	Gly	Asp	Arg	Ile	Leu	Lys	Leu	Asn	Thr	Glu	Val	
			155					160					165			
CGC	GAG	GTG	GGA	CCT	GTT	AGT	AAG	AAG	GGC	TTT	TAC	TTG	GCT	TTC	CAA	580
Arg	Glu	Val	Gly	Pro	Val	Ser	Lys	Lys	Gly	Phe	Tyr	Leu	Ala	Phe	Gln	
		170					175					180				
GAT	GTA	GGT	GCA	TGT	GTT	GCC	TTA	GTC	TCG	GTG	CGA	GTG	TAC	TTC	AAG	628
Asp	Val	Gly	Ala	Cys	Val	Ala	Leu	Val	Ser	Val	Arg	Val	Tyr	Phe	Lys	
	185					190					195					
AAG	TGC	CCT	TTC	ACT	GTC	AAG	AAC	CTC	GCC	ATG	TTT	CCA	GAT	ACA	GTT	676
Lys	Cys	Pro	Phe	Thr	Val	Lys	Asn	Leu	Ala	Met	Phe	Pro	Asp	Thr	Val	
	200			205						210					215	
CCT	ATG	GAC	TCC	CAG	TCC	CTG	GTG	GAG	GTG	CGG	GGT	TCT	TGT	GTC	AAT	724
Pro	Met	Asp	Ser	Gln	Ser	Leu	Val	Glu	Val	Arg	Gly	Ser	Cys	Val	Asn	
				220					225					230		
CAT	TCC	AAG	GAG	GAA	GAG	CCA	CCC	AAG	ATG	TAC	TGC	AGC	ACG	GAA	GGA	772
His	Ser	Lys	Glu	Glu	Glu	Pro	Pro	Lys	Met	Tyr	Cys	Ser	Thr	Glu	Gly	
			235					240					245			
GAA	TGG	CTA	GTG	CCC	ATA	GGG	AAG	TGC	TTG	TGT	AAT	GCT	GGC	TAT	GAA	820
Glu	Trp	Leu	Val	Pro	Ile	Gly	Lys	Cys	Leu	Cys	Asn	Ala	Gly	Tyr	Glu	
		250					255					260				
GAG	AGA	GGC	TTT	GCG	TGC	CAA	GCT	TGT	CGA	CCT	GGG	TTC	TAT	AAA	GCT	868
Glu	Arg	Gly	Phe	Ala	Cys	Gln	Ala	Cys	Arg	Pro	Gly	Phe	Tyr	Lys	Ala	
	265					270					275					
TCT	GCT	GGC	AAT	GTG	AAG	TGT	GCC	AAA	TGC	CCA	CCT	CAC	AGC	TCT	ACC	916
Ser	Ala	Gly	Asn	Val	Lys	Cys	Ala	Lys	Cys	Pro	Pro	His	Ser	Ser	Thr	
	280				285					290					295	
TAT	GAA	GAT	GCA	TCT	CTG	AAC	TGC	AGG	TGT	GAA	AAG	AAT	TAC	TTT	CGC	964
Tyr	Glu	Asp	Ala	Ser	Leu	Asn	Cys	Arg	Cys	Glu	Lys	Asn	Tyr	Phe	Arg	
				300					305					310		
TCT	GAG	AAA	GAC	CCT	CCA	TCC	ATG	GCT	TGC	ACC	AGA	CCA	CCA	TCT	GCT	1012
Ser	Glu	Lys	Asp	Pro	Pro	Ser	Met	Ala	Cys	Thr	Arg	Pro	Pro	Ser	Ala	
			315					320					325			



CCA	AGA	AAC	GTT	ATT	TCT	AAC	ATC	AAT	GAG	ACA	TCT	GTT	ATT	CTG	GAC	1060
Pro	Arg	Asn	Val	Ile	Ser	Asn	Ile	Asn	Glu	Thr	Ser	Val	Ile	Leu	Asp	
		330					335					340				
TGG	AGC	TGG	CCT	CTT	GAT	ACA	GGA	GGT	CGA	AAA	GAT	GTC	ACT	TTC	AAC	1108
Trp	Ser	Trp	Pro	Leu	Asp	Thr	Gly	Gly	Arg	Lys	Asp	Val	Thr	Phe	Asn	
	345					350					355					
ATC	ATT	TGC	AAA	AAA	TGT	GGA	GGA	AGC	AGC	AAG	ATA	TGT	GAG	CCT	TGC	1156
Ile	Ile	Cys	Lys	Lys	Cys	Gly	Gly	Ser	Ser	Lys	Ile	Cys	Glu	Pro	Cys	
360					365					370					375	
AGT	GAC	AAC	GTA	CGG	TTC	TTA	CCC	CGT	CAG	ACT	GGC	CTC	ACC	AAC	ACC	1204
Ser	Asp	Asn	Val	Arg	Phe	Leu	Pro	Arg	Gln	Thr	Gly	Leu	Thr	Asn	Thr	
				380					385					390		
ACG	GTG	ACA	GTA	GTG	GAC	CTT	TTG	GCA	CAT	ACC	AAT	TAC	ACT	TTT	GAG	1252
Thr	Val	Thr	Val	Val	Asp	Leu	Leu	Ala	His	Thr	Asn	Tyr	Thr	Phe	Glu	
			395					400					405			
ATT	GAT	GCA	GTC	AAC	GGG	GTA	TCT	GAC	TTG	AGT	ACA	CTT	TCG	AGA	CAA	1300
Ile	Asp	Ala	Val	Asn	Gly	Val	Ser	Asp	Leu	Ser	Thr	Leu	Ser	Arg	Gln	
		410					415					420				
TTT	GCT	GCT	GTC	AGC	ATC	ACG	ACT	AAT	CAG	GCT	GCG	CCA	TCC	CCC	ATC	1348
Phe	Ala	Ala	Val	Ser	Ile	Thr	Thr	Asn	Gln	Ala	Ala	Pro	Ser	Pro	Ile	
	425					430					435					
ACA	GTG	ATA	AGG	AAC	GAC	CGG	ACA	TCC	AGG	AAC	AGC	GTG	TCT	CTG	TCT	1396
Thr	Val	Ile	Arg	Asn	Asp	Arg	Thr	Ser	Arg	Asn	Ser	Val	Ser	Leu	Ser	
440					445					450					455	
TGG	CAG	GAG	CCT	GAG	CAC	CCA	AAT	GGA	ATC	ATC	TTG	GAC	TAC	GAG	GTC	1444
Trp	Gln	Glu	Pro	Glu	His	Pro	Asn	Gly	Ile	Ile	Leu	Asp	Tyr	Glu	Val	
				460					465					470		
AAA	TAC	TAC	GAA	AAG	CAG	GAA	CAA	GAG	ACA	AGC	TAT	ACT	ATT	CTG	AGA	1492
Lys	Tyr	Tyr	Glu	Lys	Gln	Glu	Gln	Glu	Thr	Ser	Tyr	Thr	Ile	Leu	Arg	
			475					480					485			
GCC	AAA	AGC	ACT	AAC	GTT	ACT	ATC	AGC	GGC	CTC	AAA	CCT	GAT	ACC	ACC	1540
Ala	Lys	Ser	Thr	Asn	Val	Thr	Ile	Ser	Gly	Leu	Lys	Pro	Asp	Thr	Thr	
		490					495					500				
TAC	GTC	TTC	CAA	ATT	CGA	GCC	CGA	ACT	GCA	GCT	AGA	TAT	GGG	ACA	AGC	1588
Tyr	Val	Phe	Gln	Ile	Arg	Ala	Arg	Thr	Ala	Ala	Arg	Tyr	Gly	Thr	Ser	
	505					510					515					
AGC	CGC	AAG	TTT	GAA	TTT	GAA	ACC	AGT	CCA	GAT	TCA	TTC	TCC	ATT	TCC	1636
Ser	Arg	Lys	Phe	Glu	Phe	Glu	Thr	Ser	Pro	Asp	Ser	Phe	Ser	Ile	Ser	
520					525					530					535	
AGT	GAA	AAT	AGC	CAG	GTC	GTT	ATG	ATT	GCC	ATT	TCA	GCT	GCA	GTT	GCC	1684
Ser	Glu	Asn	Ser	Gln	Val	Val	Met	Ile	Ala	Ile	Ser	Ala	Ala	Val	Ala	
				540					545					550		
ATC	ATT	CTC	CTC	ACG	GTT	GTT	GTG	TAC	GTC	TTG	ATT	GGG	AGA	TTC	TGC	1732
Ile	Ile	Leu	Leu	Thr	Val	Val	Val	Tyr	Val	Leu	Ile	Gly	Arg	Phe	Cys	
			555				560						565			
GGA	TAC	AAG	AAG	TCT	AAA	CAT	GGT	ACC	GAT	GAG	AAA	AGA	CTA	CAT	TTT	1780
Gly	Tyr	Lys	Lys	Ser	Lys	His	Gly	Thr	Asp	Glu	Lys	Arg	Leu	His	Phe	
		570					575					580				
GGG	AAT	GGC	CAC	TTA	AAA	CTC	CCA	GGC	CTG	AGA	ACT	TAT	GTA	GAT	CCA	1828
Gly	Asn	Gly	His	Leu	Lys	Leu	Pro	Gly	Leu	Arg	Thr	Tyr	Val	Asp	Pro	
	585					590					595					

CAT His 600	ACG Thr	TAC Tyr	GAA Glu	GAT Asp	CCC Pro 605	AAT Asn	CAA Gln	GCT Ala	GTA Val	CAT His 610	GAA Glu	TTT Phe	GCC Ala	AAG Lys	GAA Glu 615	1876
CTA Leu	GAT Asp	GCT Ala	TCT Ser	AAT Asn 620	ATA Ile	TCA Ser	ATT Ile	GAT Asp	AAA Lys 625	GTT Val	GTT Val	GGA Gly	GCA Ala	GGG Gly 630	GAA Glu	1924
TTT Phe	GGA Gly	GAA Glu	GTG Val 635	TGC Cys	AGT Ser	GGG Gly	CGC Arg	CTG Leu 640	AAG Lys	CTG Leu	CCT Pro	TCT Ser	AAA Lys 645	AAG Lys	GAA Glu	1972
ATT Ile	TCA Ser 650	GTG Val	GCC Ala	ATC Ile	AAA Lys	ACT Thr	CTG Leu 655	AAA Lys	GCT Ala	GGC Gly	TAC Tyr	ACA Thr 660	GAA Glu	AAA Lys	CAG Gln	2020
AGA Arg 665	AGG Arg	GAT Asp	TTC Phe	CTG Leu	GGA Gly	GAA Glu 670	GCA Ala	AGC Ser	ATC Ile	ATG Met	GGG Gly 675	CAG Gln	TTT Phe	GAC Asp	CAC His	2068
CCC Pro 680	AAC Asn	ATC Ile	ATC Ile	CGA Arg 685	CTG Leu	GAG Glu 685	GGC Gly	GTT Val	GTG Val	ACT Thr 690	AAA Lys	AGT Ser	AAA Lys	CCA Pro	GTT Val 695	2116
ATG Met	ATT Ile	GTT Val	ACT Thr 700	GAA Glu	TAC Tyr	ATG Met	GAA Glu	AAC Asn 705	GGT Gly	TCC Ser	TTG Leu	GAC Asp	AGC Ser	TTC Phe 710	CTA Leu	2164
CGG Arg	AAA Lys	CAT His 715	GAT Asp	GCC Ala	CAG Gln	TTC Phe	ACA Thr 720	GTC Val	ATT Ile	CAG Gln	CTA Leu	GTA Val	GGC Gly 725	ATG Met	CTT Leu	2212
CGT Arg	GGG Gly 730	ATC Ile	GCA Ala	TCT Ser	GGC Gly	ATG Met	AAA Lys 735	TAT Tyr	TTG Leu	TCA Ser	GAT Asp 740	ATG Met	GGT Gly	TAT Tyr	GTC Val	2260
CAC His 745	CGA Arg	GAT Asp	CTA Leu	GCT Ala	GCT Ala	CGT Arg 750	AAT Asn	ATA Ile	CTC Leu	ATC Ile	AAT Asn 755	AGT Ser	AAC Asn	TTG Leu	GTG Val	2308
TGC Cys 760	AAA Lys	GTC Val	TCA Ser	GAT Asp 765	TTT Phe	GGT Gly	CTT Leu	TCT Ser	CGT Arg 770	GTA Val	TTG Leu	GAA Glu	GAT Asp	GAC Asp	CCA Pro 775	2356
GAA Glu	GCT Ala	GCT Ala	TAC Tyr 780	ACA Thr	ACA Thr	AGG Arg	GGG Gly	GGC Gly	AAG Lys 785	ATT Ile	CCC Pro	ATC Ile	CGA Arg	TGG Trp 790	ACG Thr	2404
TCA Ser	CCA Pro	GAA Glu 795	GCC Ala	ATT Ile	GCA Ala	TAC Tyr	CGG Arg 800	AAG Lys	TTC Phe	ACA Thr	TCA Ser	GCC Ala 805	AGT Ser	GAT Asp	GCG Ala	2452
TGG Trp	AGC Ser	TAT Tyr 810	GGG Gly	ATT Ile	GTC Val	CTC Leu	TGG Trp 815	GAG Glu	GTG Val	ATG Met	TCT Ser	TAT Tyr 820	GGA Gly	GAA Glu	AGG Arg	2500
CCG Pro 825	TAC Tyr	TGG Trp	GAG Glu	ATG Met	TCC Ser	TTC Phe 830	CAG Gln	GAC Asp	GTA Val	ATT Ile	AAA Lys 835	GCC Ala	GTT Val	GAT Asp	GAA Glu	2548
GGG Gly 840	TAT Tyr	CGC Arg	TTG Leu	CCA Pro	CCT Pro 845	CCT Pro	ATG Met	GAC Asp	TGC Cys	CCA Pro 850	GCT Ala	GCC Ala	TTG Leu	TAT Tyr	CAG Gln 855	2596
CTG Leu	ATG Met	CTG Leu	GAC Asp 860	TGC Cys	TGG Trp	CAG Gln	AAA Lys	GAC Asp	AGA Arg 865	AAC Asn	AAC Asn	AGA Arg	CCC Pro	AAG Lys 870	TTT Phe	2644

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GAG CAG ATT GTC AGC ATC CTG GAT AAG CTG ATC CGT AAT CCC AGC AGT	2692
Glu Gln Ile Val Ser Ile Leu Asp Lys Leu Ile Arg Asn Pro Ser Ser	
875 880 885	
CTG AAA ATA ATC ACC AAT GCG GCA GCA AGG CCA TCA AAT CTT CTC CTG	2740
Leu Lys Ile Ile Thr Asn Ala Ala Arg Pro Ser Asn Leu Leu Leu	
890 895 900	
GAC CAA AGT AAC ATT GAC ATT TCA GCG TTC CGC ACG GCA GGT GAT TGG	2788
Asp Gln Ser Asn Ile Asp Ile Ser Ala Phe Arg Thr Ala Gly Asp Trp	
905 910 915	
CTC AAT GGT TTT CGA ACA GGA CAG TGC AAA GGC ATT TTC ACG GGT GTG	2836
Leu Asn Gly Phe Arg Thr Gly Gln Cys Lys Gly Ile Phe Thr Gly Val	
920 925 930 935	
GAG TAC AGC TCC TGT GAT ACA ATA GCC AAG ATT TCC ACT GAT GAC ATG	2884
Glu Tyr Ser Ser Cys Asp Thr Ile Ala Lys Ile Ser Thr Asp Asp Met	
940 945 950	
AAG AAA GTT GGT GTT ACA GTT GTG GGG CCT CAA AAG AAG ATT GTT AGC	2932
Lys Lys Val Gly Val Thr Val Val Gly Pro Gln Lys Lys Ile Val Ser	
955 960 965	
AGT ATC AAA ACT CTA GAA ACT CAT ACG AAG AAC AGC CCT GTT CCT GTG	2980
Ser Ile Lys Thr Leu Glu Thr His Thr Lys Asn Ser Pro Val Pro Val	
970 975 980	
TAAGGTACCA AAATGATGTT GCTGAGGACA GAAAAAAAAG AAAAGTCGCA TCAAAGTGCA	3040
AAAGCGATGG CTGATAAACG GCACGGTTTA AAGGAGTTCT TTGCAGCAGT TTTGGAAACA	3100
TAATGGTTGA AATTTCAAAC CCACTGAGAC ACTCAAATAC TGAGTATAAA TGCCTTAAAA	3160
ATAGGAGCGA ACTTGTTTTTC TATCTGTTAA TCCTGAAGGG TGGGTGCTCT TAACTGACTG	3220
TTAATGCAGA TAGTAAATTT CAAAAA AAAA AACG	3254

## (2) INFORMATION FOR SEQ ID NO:16:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 983 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: protein

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

Met Asp Arg Arg Arg Leu Pro Leu Leu Leu Cys Ala Ala Leu Gly  
1 5 10 15

Ser Ala Gly Arg Leu Ser Ala Arg Pro Gly Asn Glu Val Asn Leu Leu  
20 25 30

Asp Ser Lys Thr Ile Gln Gly Glu Leu Gly Trp Ile Ser Tyr Pro Ser  
35 40 45

His Gly Trp Glu Glu Ile Ser Gly Val Asp Glu His Tyr Thr Pro Ile  
50 55 60

Arg Thr Tyr Gln Glu Ser Asn Val Met Asp His Ser Gln Asn Asn Trp  
65 70 75 80

Leu Arg Thr Asn Trp Ile Pro Arg Asn Ser Ala Gln Lys Ile Tyr Val  
85 90 95

Glu Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Ile Pro Leu Val Leu  
 100 105 110  
 Gly Thr Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Met Glu Ser Asp Asp  
 115 120 125  
 Asp His Leu Ala Lys Phe Arg Glu His Gln Phe Thr Lys Ile Asp Thr  
 130 135 140  
 Met Ala Ala Asp Glu Ser Phe Thr Gln Met Asp Leu Gly Asp Arg Ile  
 145 150 155 160  
 Leu Lys Leu Asn Thr Glu Val Arg Glu Val Gly Pro Val Ser Lys Lys  
 165 170 175  
 Gly Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Val Ala Leu Val  
 180 185 190  
 Ser Val Arg Val Tyr Phe Lys Lys Cys Pro Phe Thr Val Lys Asn Leu  
 195 200 205  
 Ala Met Phe Pro Asp Thr Val Pro Met Asp Ser Gln Ser Leu Val Glu  
 210 215 220  
 Val Arg Gly Ser Cys Val Asn His Ser Lys Glu Glu Glu Pro Pro Lys  
 225 230 235 240  
 Met Tyr Cys Ser Thr Glu Gly Glu Trp Leu Val Pro Ile Gly Lys Cys  
 245 250 255  
 Leu Cys Asn Ala Gly Tyr Glu Glu Arg Gly Phe Ala Cys Gln Ala Cys  
 260 265 270  
 Arg Pro Gly Phe Tyr Lys Ala Ser Ala Gly Asn Val Lys Cys Ala Lys  
 275 280 285  
 Cys Pro Pro His Ser Ser Thr Tyr Glu Asp Ala Ser Leu Asn Cys Arg  
 290 295 300  
 Cys Glu Lys Asn Tyr Phe Arg Ser Glu Lys Asp Pro Pro Ser Met Ala  
 305 310 315 320  
 Cys Thr Arg Pro Pro Ser Ala Pro Arg Asn Val Ile Ser Asn Ile Asn  
 325 330 335  
 Glu Thr Ser Val Ile Leu Asp Trp Ser Trp Pro Leu Asp Thr Gly Gly  
 340 345 350  
 Arg Lys Asp Val Thr Phe Asn Ile Ile Cys Lys Lys Cys Gly Gly Ser  
 355 360 365  
 Ser Lys Ile Cys Glu Pro Cys Ser Asp Asn Val Arg Phe Leu Pro Arg  
 370 375 380  
 Gln Thr Gly Leu Thr Asn Thr Thr Val Thr Val Val Asp Leu Leu Ala  
 385 390 395 400  
 His Thr Asn Tyr Thr Phe Glu Ile Asp Ala Val Asn Gly Val Ser Asp  
 405 410 415  
 Leu Ser Thr Leu Ser Arg Gln Phe Ala Ala Val Ser Ile Thr Thr Asn  
 420 425 430  
 Gln Ala Ala Pro Ser Pro Ile Thr Val Ile Arg Asn Asp Arg Thr Ser  
 435 440 445

Arg Asn Ser Val Ser Leu Ser Trp Gln Glu Pro Glu His Pro Asn Gly  
 450 455 460  
 Ile Ile Leu Asp Tyr Glu Val Lys Tyr Tyr Glu Lys Gln Glu Gln Glu  
 465 470 475 480  
 Thr Ser Tyr Thr Ile Leu Arg Ala Lys Ser Thr Asn Val Thr Ile Ser  
 485 490 495  
 Gly Leu Lys Pro Asp Thr Thr Tyr Val Phe Gln Ile Arg Ala Arg Thr  
 500 505 510  
 Ala Ala Arg Tyr Gly Thr Ser Ser Arg Lys Phe Glu Phe Glu Thr Ser  
 515 520 525  
 Pro Asp Ser Phe Ser Ile Ser Ser Glu Asn Ser Gln Val Val Met Ile  
 530 535 540  
 Ala Ile Ser Ala Ala Val Ala Ile Ile Leu Leu Thr Val Val Val Tyr  
 545 550 555 560  
 Val Leu Ile Gly Arg Phe Cys Gly Tyr Lys Lys Ser Lys His Gly Thr  
 565 570 575  
 Asp Glu Lys Arg Leu His Phe Gly Asn Gly His Leu Lys Leu Pro Gly  
 580 585 590  
 Leu Arg Thr Tyr Val Asp Pro His Thr Tyr Glu Asp Pro Asn Gln Ala  
 595 600 605  
 Val His Glu Phe Ala Lys Glu Leu Asp Ala Ser Asn Ile Ser Ile Asp  
 610 615 620  
 Lys Val Val Gly Ala Gly Glu Phe Gly Glu Val Cys Ser Gly Arg Leu  
 625 630 635 640  
 Lys Leu Pro Ser Lys Lys Glu Ile Ser Val Ala Ile Lys Thr Leu Lys  
 645 650 655  
 Ala Gly Tyr Thr Glu Lys Gln Arg Arg Asp Phe Leu Gly Glu Ala Ser  
 660 665 670  
 Ile Met Gly Gln Phe Asp His Pro Asn Ile Ile Arg Leu Glu Gly Val  
 675 680 685  
 Val Thr Lys Ser Lys Pro Val Met Ile Val Thr Glu Tyr Met Glu Asn  
 690 695 700  
 Gly Ser Leu Asp Ser Phe Leu Arg Lys His Asp Ala Gln Phe Thr Val  
 705 710 715 720  
 Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ser Gly Met Lys Tyr  
 725 730 735  
 Leu Ser Asp Met Gly Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile  
 740 745 750  
 Leu Ile Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser  
 755 760 765  
 Arg Val Leu Glu Asp Asp Pro Glu Ala Ala Tyr Thr Thr Arg Gly Gly  
 770 775 780  
 Lys Ile Pro Ile Arg Trp Thr Ser Pro Glu Ala Ile Ala Tyr Arg Lys  
 785 790 795 800

Phe	Thr	Ser	Ala	Ser 805	Asp	Ala	Trp	Ser	Tyr 810	Gly	Ile	Val	Leu	Trp 815	Glu
Val	Met	Ser	Tyr 820	Gly	Glu	Arg	Pro	Tyr 825	Trp	Glu	Met	Ser	Phe 830	Gln	Asp
Val	Ile	Lys 835	Ala	Val	Asp	Glu	Gly 840	Tyr	Arg	Leu	Pro	Pro 845	Pro	Met	Asp
Cys	Pro 850	Ala	Ala	Leu	Tyr	Gln 855	Leu	Met	Leu	Asp	Cys 860	Trp	Gln	Lys	Asp
Arg 865	Asn	Asn	Arg	Pro	Lys 870	Phe	Glu	Gln	Ile	Val 875	Ser	Ile	Leu	Asp	Lys 880
Leu	Ile	Arg	Asn	Pro 885	Ser	Ser	Leu	Lys	Ile 890	Ile	Thr	Asn	Ala	Ala 895	Ala
Arg	Pro	Ser	Asn 900	Leu	Leu	Leu	Asp	Gln 905	Ser	Asn	Ile	Asp	Ile 910	Ser	Ala
Phe	Arg	Thr 915	Ala	Gly	Asp	Trp	Leu 920	Asn	Gly	Phe	Arg	Thr 925	Gly	Gln	Cys
Lys 930	Gly	Ile	Phe	Thr	Gly	Val 935	Glu	Tyr	Ser	Ser	Cys 940	Asp	Thr	Ile	Ala
Lys 945	Ile	Ser	Thr	Asp	Asp 950	Met	Lys	Lys	Val	Gly 955	Val	Thr	Val	Val	Gly 960
Pro	Gln	Lys	Lys	Ile 965	Val	Ser	Ser	Ile	Lys 970	Thr	Leu	Glu	Thr	His 975	Thr
Lys	Asn	Ser	Pro 980	Val	Pro	Val									

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 4049 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: both  
(D) TOPOLOGY: linear

(ix) FEATURE:

- (A) NAME/KEY: CDS  
(B) LOCATION: 10..2994

(xi) SEQUENCE DESCRIPTION: SEO ID NO:17:

CGGCTTCTG	ATG	CCC	GGC	CCG	GAG	CGC	ACC	ATG	GGG	CCG	TTG	TGG	TTC		48	
	Met	Pro	Gly	Pro	Glu	Arg	Thr	Met	Gly	Pro	Leu	Trp	Phe			
	1				5					10						
TGC	TGT	TTG	CCC	CTC	GCC	CTC	TTG	CCT	CTG	CTC	GCC	GCC	GTG	GAA	GAG	96
Cys	Cys	Leu	Pro	Leu	Ala	Leu	Leu	Pro	Leu	Leu	Ala	Ala	Val	Glu	Glu	
	15					20					25					
ACG	CTG	ATG	GAC	TCC	ACA	ACG	GCC	ACA	GCA	GAG	CTG	GGC	TGG	ATG	GTG	144
Thr	Leu	Met	Asp	Ser	Thr	Thr	Ala	Thr	Ala	Glu	Leu	Gly	Trp	Met	Val	
	30				35					40					45	
CAT	CCT	CCC	TCA	GGG	TGG	GAA	GAG	GTG	AGT	GGA	TAC	GAT	GAG	AAC	ATG	192
His	Pro	Pro	Ser	Gly	Trp	Glu	Glu	Val	Ser	Gly	Tyr	Asp	Glu	Asn	Met	
				50					55					60		

AAC ACC ATC CGC ACC TAC CAG GTG TGC AAC GTC TTT GAA TCC AGC CAA	240
Asn Thr Ile Arg Thr Tyr Gln Val Cys Asn Val Phe Glu Ser Ser Gln	
65 70 75	
AAC AAC TGG CTG CGG ACC AAG TAC ATC CGG AGG CGA GGA GCG CAC CGC	288
Asn Asn Trp Leu Arg Thr Lys Tyr Ile Arg Arg Arg Gly Ala His Arg	
80 85 90	
ATC CAC GTG GAG ATG AAA TTC TCC GTT CGG GAC TGC AGC AGC ATC CCC	336
Ile His Val Glu Met Lys Phe Ser Val Arg Asp Cys Ser Ser Ile Pro	
95 100 105	
AAC GTC CCG GGC TCC TGT AAG GAG ACT TTT AAC CTC TAT TAC TAC GAA	384
Asn Val Pro Gly Ser Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Tyr Glu	
110 115 120 125	
TCA GAC TTT GAC TCT GCC ACC AAG ACT TTT CCT AAC TGG ATG GAA AAC	432
Ser Asp Phe Asp TCT Ala Thr Lys Thr Phe Pro Asn Trp Met Glu Asn	
130 135 140	
CCT TGG ATG AAG GTA GAT ACA ATT GCT GCC GAC GAG AGC TTC TCG CAG	480
Pro Trp Met Lys Val Asp Thr Ile Ala Ala Asp Glu Ser Phe Ser Gln	
145 150 155	
GTG GAC CTT GGT GGG CGG GTG ATG AAG ATT AAC ACC GAG GTG CGC AGT	528
Val Asp Leu Gly Gly Arg Val Met Lys Ile Asn Thr Glu Val Arg Ser	
160 165 170	
TTT GGG CCT GTC TCC AAA AAC GGT TTC TAC CTG GCC TTC CAG GAC TAC	576
Phe Gly Pro Val Ser Lys Asn Gly Phe Tyr Leu Ala Phe Gln Asp Tyr	
175 180 185	
GGG GGC TGC ATG TCC TTG ATT GCA GTC CGT GTC TTT TAC CGC AAG TGT	624
Gly Gly Cys Met Ser Leu Ile Ala Val Arg Val Phe Tyr Arg Lys Cys	
190 195 200 205	
CCC CGT GTG ATC CAG AAC GGG GCG GTC TTC CAG GAA ACC CTC TCG GGA	672
Pro Arg Val Ile Gln Asn Gly Ala Val Phe Gln Glu Thr Leu Ser Gly	
210 215 220	
GCG GAG AGC ACA TCT CTG GTG GCA GCC CGG GGG ACG TGC ATC AGC AAT	720
Ala Glu Ser Thr Ser Leu Val Ala Ala Arg Gly Thr Cys Ile Ser Asn	
225 230 235	
GCG GAG GAG GTG GAT GTG CCC ATC AAG CTG TAC TGC AAT GGG GAT GGC	768
Ala Glu Glu Val Asp Val Pro Ile Lys Leu Tyr Cys Asn Gly Asp Gly	
240 245 250	
GAG TGG CTG GTG CCC ATC GGC CGC TGC ATG TGC AGG CCG GGC TAT GAG	816
Glu Trp Leu Val Pro Ile Gly Arg Cys Met Cys Arg Pro Gly Tyr Glu	
255 260 265	
TCG GTG GAG AAT GGG ACC GTC TGC AGA GGC TGC CCA TCA GGG ACC TTC	864
Ser Val Glu Asn Gly Thr Val Cys Arg Gly Cys Pro Ser Gly Thr Phe	
270 275 280 285	
AAG GCC AGC CAA GGA GAT GAA GGA TGT GTC CAT TGT CCA ATT AAC AGC	912
Lys Ala Ser Gln Gly Asp Glu Gly Cys Val His Cys Pro Ile Asn Ser	
290 295 300	
CGG ACG ACT TCG GAA GGG GCC ACG AAC TGC GTG TGC CGA AAC GGA TAT	960
Arg Thr Thr Ser Glu Gly Ala Thr Asn Cys Val Cys Arg Asn Gly Tyr	
305 310 315	
TAC CGG GCA GAT GCT GAC CCC GTC GAC ATG CCA TGC ACC ACC ATC CCA	1008
Tyr Arg Ala Asp Ala Asp Pro Val Asp Met Pro Cys Thr Thr Ile Pro	
320 325 330	

TCT	GCC	CCC	CAG	GCC	GTG	ATC	TCC	AGC	GTG	AAT	GAA	ACC	TCC	CTG	ATG	1056
Ser	Ala	Pro	Gln	Ala	Val	Ile	Ser	Ser	Val	Asn	Glu	Thr	Ser	Leu	Met	
	335					340					345					
CTG	GAG	TGG	ACC	CCA	CCA	CGA	GAC	TCA	GGG	GGC	CGG	GAG	GAT	CTG	GTA	1104
Leu	Glu	Trp	Thr	Pro	Pro	Arg	Asp	Ser	Gly	Gly	Arg	Glu	Asp	Leu	Val	
	350				355					360					365	
TAC	AAC	ATC	ATC	TGC	AAG	AGC	TGT	GGG	TCA	GGC	CGT	GGG	GCG	TGC	ACG	1152
Tyr	Asn	Ile	Ile	Cys	Lys	Ser	Cys	Gly	Ser	Gly	Arg	Gly	Ala	Cys	Thr	
				370					375					380		
CGC	TGT	GGG	GAC	AAC	GTG	CAG	TTT	GCC	CCA	CGC	CAG	CTG	GGC	CTG	ACG	1200
Arg	Cys	Gly	Asp	Asn	Val	Gln	Phe		Pro	Arg	Gln	Leu	Gly	Leu	Thr	
			385					390					395			
GAG	CCT	CGC	ATC	TAC	ATC	AGC	GAC	CTG	CTG	GCC	CAC	ACG	CAG	TAC	ACC	1248
Glu	Pro	Arg	Ile	Tyr	Ile	Ser	Asp	Leu	Leu	Ala	His		Gln	Tyr	Thr	
	400						405					410				
TTT	GAG	ATC	CAG	GCT	GTG	AAT	GGG	GTC	ACC	GAC	CAG	AGC	CCC	TTC	TCC	1296
Phe	Glu	Ile	Gln	Ala	Val	Asn	Gly	Val	Thr	Asp	Gln	Ser	Pro	Phe	Ser	
	415					420					425					
CCA	CAG	TTT	GCA	TCA	GTG	AAT	ATC	ACC	ACC	AAC	CAG	GCT	GCT	CCT	TCA	1344
Pro	Gln	Phe	Ala	Ser	Val	Asn	Ile	Thr	Thr	Asn	Gln	Ala	Ala	Pro	Ser	
	430				435					440					445	
GCC	GTG	TCC	ATA	ATG	CAC	CAG	GTC	AGC	CGC	ACT	GTG	GAC	AGC	ATT	ACC	1392
Ala	Val	Ser	Ile	Met	His	Gln	Val	Ser	Arg	Thr	Val	Asp	Ser	Ile	Thr	
				450					455					460		
CTC	TCG	TGG	TCT	CAA	CCT	GAC	CAG	CCC	AAT	GGA	GTC	ATC	CTG	GAT	TAT	1440
Leu	Ser	Trp	Ser	Gln	Pro	Asp	Gln	Pro	Asn	Gly	Val	Ile	Leu	Asp	Tyr	
			465					470					475			
GAG	CTG	CAA	TAC	TAT	GAG	AAG	AAC	CTG	AGT	GAG	TTA	AAT	TCA	ACA	GCA	1488
Glu	Leu	Gln	Tyr	Tyr	Glu	Lys	Asn	Leu	Ser	Glu	Leu	Asn	Ser	Thr	Ala	
		480					485					490				
GTG	AAG	AGC	CCC	ACC	AAC	ACT	GTG	ACA	GTG	CAA	AAC	CTC	AAA	GCT	GGC	1536
Val	Lys	Ser	Pro	Thr	Asn	Thr	Val	Thr	Val	Gln	Asn	Leu	Lys	Ala	Gly	
	495					500					505					
ACC	ATC	TAT	GTC	TTC	CAA	GTG	CGA	GCA	CGT	ACC	GTG	GCT	GGG	TAT	GGC	1584
Thr	Ile	Tyr	Val	Phe	Gln	Val	Arg	Ala	Arg	Thr	Val	Ala	Gly	Tyr	Gly	
	510				515					520					525	
CGG	TAT	AGT	GGC	AAG	ATG	TAC	TTC	CAG	ACC	ATG	ACT	GAA	GCC	GAG	TAC	1632
Arg	Tyr	Ser	Gly	Lys	Met	Tyr	Phe	Gln	Thr	Met	Thr	Glu	Ala	Glu	Tyr	
				530					535					540		
CAG	ACC	AGT	GTC	CAG	GAG	AAG	CTG	CCA	CTC	ATC	ATT	GGC	TCC	TCT	GCA	1680
Gln	Thr	Ser	Val	Gln	Glu	Lys	Leu	Pro	Leu	Ile	Ile	Gly	Ser	Ser	Ala	
			545					550					555			
GCA	GGA	CTG	GTG	TTT	CTC	ATT	GCT	GTT	GTC	GTC	ATC	ATT	ATT	GTC	TGC	1728
Ala	Gly	Leu	Val	Phe	Leu	Ile	Ala	Val	Val	Val	Ile	Ile	Ile	Val	Cys	
		560					565					570				
AAC	AGA	AGA	CGG	GGC	TTT	GAA	CGT	GCT	GAC	TCT	GAG	TAC	ACT	GAC	AAG	1776
Asn	Arg	Arg	Arg	Gly	Phe	Glu	Arg	Ala	Asp	Ser	Glu	Tyr	Thr	Asp	Lys	
	575					580					585					
CTG	CAG	CAC	TAT	ACC	AGT	GGC	CAC	ATG	ACT	CCA	GGG	ATG	AAG	ATT	TAT	1824
Leu	Gln	His	Tyr	Thr	Ser	Gly	His	Met	Thr	Pro	Gly	Met	Lys	Ile	Tyr	
	590				595					600					605	



ATC Ile	GAT Asp	CCA Pro	TTT Phe	ACC Thr 610	TAC Tyr	GAA Glu	GAT Asp	CCC Pro	AAT Asn 615	GAG Glu	GCT Ala	GTC Val	AGG Arg	GAA Glu 620	TTT Phe	1872
GCA Ala	AAA Lys	GAA Glu	ATT Ile 625	GAT Asp	ATC Ile	TCC Ser	TGT Cys	GTG Val 630	AAA Lys	ATC Ile	GAG Glu	CAG Gln	GTG Val 635	ATT Ile	GGG Gly	1920
GCA Ala	GGG Gly	GAG Phe 640	TTT Phe	GGT Gly	GAG Glu	GTG Val	TGC Cys 645	AGT Ser	GGG Gly	CAT His	CTC Leu	AAG Lys 650	CTT Leu	CCT Pro	GGC Gly	1968
AAA Lys	AGA Arg 655	GAG Glu	ATC Ile	TTT Phe	GTG Val	GCC Ala 660	ATC Ile	AAG Lys	ACC Thr	CTG Leu	AAG Lys 665	TCT Ser	GGT Gly	TAC Tyr	ACA Thr	2016
GAG Glu 670	AAG Lys	CAG Gln	AGA Arg	CGG Arg	GAC Asp 675	TTC Phe	CTG Leu	AGT Ser	GAA Glu	GCC Ala 680	AGC Ser	ATC Ile	ATG Met	GGG Gly	CAG Gln 685	2064
TTT Phe	GAC Asp	CAC His	CCC Pro	AAT Asn 690	GTC Val	ATC Ile	CAC His	CTG Leu	GAA Glu 695	GGG Gly	GTG Val	GTG Val	ACC Thr	AAG Lys 700	AGT Ser	2112
TCC Ser	CCA Pro	GTC Val	ATG Met 705	ATC Ile	ATT Ile	ACA Thr	GAG Glu	TTC Phe 710	ATG Met	GAG Glu	AAT Asn	GGC Gly	TCG Ser 715	TTG Leu	GAC Asp	2160
TCC Ser	TTC Phe	TTG Leu 720	AGG Arg	CAA Gln	AAT Asn	GAT Asp	GGG Gly 725	CAG Gln	TTC Phe	ACA Thr	GTG Val	ATC Ile 730	CAG Gln	CTG Leu	GTG Val	2208
GGC Gly 735	ATG Met	TTG Leu	CGT Arg	GGC Gly	ATT Ile	GCA Ala 740	GCA Ala	GGC Gly	ATG Met	AAG Lys	TAC Tyr 745	CTG Leu	GCT Ala	GAT Asp	ATG Met	2256
AAC Asn 750	TAC Tyr	GTG Val	CAC His	CGG Arg	GAC Asp 755	CTG Leu	GCT Ala	GCC Ala	CGC Arg	AAC Asn 760	ATC Ile	CTG Leu	GTC Val	AAC Asn 765	AGC Ser 765	2304
AAC Asn	CTG Leu	GTC Val	TGC Cys	AAG Lys 770	GTG Val	TCC Ser	GAC Asp	TTC Phe	GGC Gly 775	CTC Leu	TCC Ser	CGT Arg	TTC Phe	CTG Leu 780	GAG Glu	2352
GAT Asp	GAC Asp	ACC Thr	TCT Ser 785	GAT Asp	CCC Pro	ACT Thr	TAC Tyr	ACC Thr 790	AGC Ser	GCA Ala	CTG Leu	GGT Gly	GGA Gly 795	AAG Lys	ATC Ile	2400
CCA Pro	ATA Ile	CGG Arg 800	TGG Trp	ACA Thr	GCG Ala	CCT Pro	GAG Glu 805	GCA Ala	ATT Ile	CAG Gln	TAC Tyr	CGA Arg 810	AAA Lys	TTC Phe	ACA Thr	2448
TCA Ser	GCC Ala 815	AGC Ser	GAT Asp	GTG Val	TGG Trp	AGC Ser 820	TAT Tyr	GGA Gly	ATA Ile	GTC Val	ATG Met 825	TGG Trp	GAG Glu	GTG Val	ATG Met	2496
TCG Ser 830	TAC Tyr	GGC Gly	GAG Glu	CGG Arg	CCT Pro 835	TAC Tyr	TGG Trp	GAC Asp	ATG Met	ACC Thr 840	AAT Asn	CAA Gln	GAT Asp	GTG Val	ATA Ile 845	2544
AAT Asn	GCT Ala	ATT Ile	GAG Glu	CAG Gln 850	GAC Asp	TAT Tyr	CGG Arg	CTA Leu	CCA Pro 855	CCC Pro	CCT Pro	ATG Met	GAT Asp	TGT Cys 860	CCA Pro	2592
AAT Asn	GCC Ala	CTG Leu	CAC His 865	CAG Gln	CTA Leu	ATG Met	CTT Leu	GAC Asp 870	TGC Cys	TGG Trp	CAG Gln	AAG Lys	GAT Asp 875	CGA Arg	AAC Asn	2640

CAC AGA CCC AAA TTT GGA CAG ATT GTC AAC ACT TTA GAC AAA ATG ATC His Arg Pro Lys Phe Gly Gln Ile Val Asn Thr Leu Asp Lys Met Ile 880 885 890	2688
CGA AAT CCT AAT AGT CTG AAA GCC ATG GCA CCT CTC TCC TCT GGG GTT Arg Asn Pro Asn Ser Leu Lys Ala Met Ala Pro Leu Ser Ser Gly Val 895 900 905	2736
AAC CTC CCT CTA CTT GAC CGC ACA ATC CCA GAT TAT ACC AGC TTC AAC Asn Leu Pro Leu Leu Asp Arg Thr Ile Pro Asp Tyr Thr Ser Phe Asn 910 915 920 925	2784
ACT GTG GAT GAA TGG CTG GAT GCC ATC AAG ATG AGC CAG TAC AAG GAG Thr Val Asp Glu Trp Leu Asp Ala Ile Lys Met Ser Gln Tyr Lys Glu 930 935 940	2832
AGC TTT GCC AGT GCT GGC TTC ACC ACC TTT GAT ATA GTA TCT CAG ATG Ser Phe Ala Ser Ala Gly Phe Thr Thr Phe Asp Ile Val Ser Gln Met 945 950 955	2880
ACT GTA GAG GAC ATT CTA CGA GTT GGG GTC ACT TTA GCA GGA CAC CAG Thr Val Glu Asp Ile Leu Arg Val Gly Val Thr Leu Ala Gly His Gln 960 965 970	2928
AAG AAA ATT CTG AAC AGT ATC CAG GTG ATG AGA GCA CAG ATG AAC CAA Lys Lys Ile Leu Asn Ser Ile Gln Val Met Arg Ala Gln Met Asn Gln 975 980 985	2976
ATT CAG TCT GTG GAG GTT TGATAGCAAC ACGTCCTCGT GCTCCACTTC Ile Gln Ser Val Glu Val 990 995	3024
CTTGAGGCCC TGCTCCCCTC TGCCCCTGTG TGTCTGAGCT CCAGTTCTTG AGTGTCTGCTG	3084
GTGGATCAGA GACAGGCAGC TGCTCTGAGG ATCATGGCAA CAGGAAGAAA TGCCCTATCA	3144
TTGACAACGA GAAGTCATCA AGAGGTGAAA CAATGGAAAA CAATGGAAAA AGGGAACAAG	3204
TAAAGACAGC TATTTTGAAG ACCGAAAACA AACAGTGAAT TATTTTAAAA TAATAATAAA	3264
GCAATTGCAG TCTTGAAAAG GGCTCCAAGA CCAATGGGAG TCTCCAAAGG AAGAGAATAG	3324
AGCAGCTTCA TCTATTTCTT CTTACACAAG GGTTGCTGCA GCTGGGCCCA GACACTTCTG	3384
GAGTAACGAG ACTTTTCAAG AAGATGAATG CAAAGAATGG TCACAAGAAG CACTTCTCTT	3444
TCTCACATGG GATGGCAGCT CTGGGAATGC CCGGCAGTCC TTCCTGAAAG CCCTGTTGGC	3504
AAATCGAAGA GGAGAGCCGA AGCTCTTTGG TGCTGTGGAA CCAAGTGCAT CTCAGAAATT	3564
GTTGGACTTC TACAAAAGCT GAAGACATTC TTTTTTTTTA AACAAGTAAA CTGATACTAG	3624
AAGAGGCTGT TTCCGTCAAA TGAGAAGGAA TCTGTAACAC TGGCCCGGGG GGGGTGGGGA	3684
ATGGGGGAAA TCAGTCCTTT TTACATCTCT TTATTTTCTC TTGTCATGGA ACAGTTTGT	3744
GAGTGACAGT TTCCTAAGGG TCCGTCCATC CACCCTCCAA TGGCATCATT GTTTCATACA	3804
TATCATATGC ACAAGACTTA TAGTGATGTC CTCACTCGAT GCCAATGATC TTTCCCCAGA	3864
AGACTTCCCA AGTACAGTAT GTAGTAGATT TTGATTACAA ATGCTGACGT GTACCTTTAT	3924
TTTTCGGTTG TCGTTGTTGG GAGATTCGTC CTTTACCTT GCTTTGTTAA CACCAATTG	3984
TGAGTTTGGG GTTGAATTT TTTTGGTCGA TTGGGGTGT TTTTTTTTTT TTTTTTTTTT	4044
AACCG	4049

## (2) INFORMATION FOR SEQ ID NO:18:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 995 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: protein

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

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Met Pro Gly Pro Glu Arg Thr Met Gly Pro Leu Trp Phe Cys Cys Leu
 1           5           10           15
Pro Leu Ala Leu Leu Pro Leu Leu Ala Ala Val Glu Glu Thr Leu Met
          20           25           30
Asp Ser Thr Thr Ala Thr Ala Glu Leu Gly Trp Met Val His Pro Pro
          35           40           45
Ser Gly Trp Glu Glu Val Ser Gly Tyr Asp Glu Asn Met Asn Thr Ile
          50           55           60
Arg Thr Tyr Gln Val Cys Asn Val Phe Glu Ser Ser Gln Asn Asn Trp
          65           70           75           80
Leu Arg Thr Lys Tyr Ile Arg Arg Arg Gly Ala His Arg Ile His Val
          85           90           95
Glu Met Lys Phe Ser Val Arg Asp Cys Ser Ser Ile Pro Asn Val Pro
          100          105          110
Gly Ser Cys Lys Glu Thr Phe Asn Leu Tyr Tyr Tyr Glu Ser Asp Phe
          115          120          125
Asp Ser Ala Thr Lys Thr Phe Pro Asn Trp Met Glu Asn Pro Trp Met
          130          135          140
Lys Val Asp Thr Ile Ala Ala Asp Glu Ser Phe Ser Gln Val Asp Leu
          145          150          155          160
Gly Gly Arg Val Met Lys Ile Asn Thr Glu Val Arg Ser Phe Gly Pro
          165          170          175
Val Ser Lys Asn Gly Phe Tyr Leu Ala Phe Gln Asp Tyr Gly Gly Cys
          180          185          190
Met Ser Leu Ile Ala Val Arg Val Phe Tyr Arg Lys Cys Pro Arg Val
          195          200          205
Ile Gln Asn Gly Ala Val Phe Gln Glu Thr Leu Ser Gly Ala Glu Ser
          210          215          220
Thr Ser Leu Val Ala Ala Arg Gly Thr Cys Ile Ser Asn Ala Glu Glu
          225          230          235          240
Val Asp Val Pro Ile Lys Leu Tyr Cys Asn Gly Asp Gly Glu Trp Leu
          245          250          255
Val Pro Ile Gly Arg Cys Met Cys Arg Pro Gly Tyr Glu Ser Val Glu
          260          265          270
Asn Gly Thr Val Cys Arg Gly Cys Pro Ser Gly Thr Phe Lys Ala Ser
          275          280          285

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Gln Gly Asp Glu Gly Cys Val His Cys Pro Ile Asn Ser Arg Thr Thr  
 290 295 300  
 Ser Glu Gly Ala Thr Asn Cys Val Cys Arg Asn Gly Tyr Tyr Arg Ala  
 305 310 315 320  
 Asp Ala Asp Pro Val Asp Met Pro Cys Thr Thr Ile Pro Ser Ala Pro  
 325 330 335  
 Gln Ala Val Ile Ser Ser Val Asn Glu Thr Ser Leu Met Leu Glu Trp  
 340 345 350  
 Thr Pro Pro Arg Asp Ser Gly Gly Arg Glu Asp Leu Val Tyr Asn Ile  
 355 360 365  
 Ile Cys Lys Ser Cys Gly Ser Gly Arg Gly Ala Cys Thr Arg Cys Gly  
 370 375 380  
 Asp Asn Val Gln Phe Ala Pro Arg Gln Leu Gly Leu Thr Glu Pro Arg  
 385 390 395 400  
 Ile Tyr Ile Ser Asp Leu Leu Ala His Thr Gln Tyr Thr Phe Glu Ile  
 405 410 415  
 Gln Ala Val Asn Gly Val Thr Asp Gln Ser Pro Phe Ser Pro Gln Phe  
 420 425 430  
 Ala Ser Val Asn Ile Thr Thr Asn Gln Ala Ala Pro Ser Ala Val Ser  
 435 440 445  
 Ile Met His Gln Val Ser Arg Thr Val Asp Ser Ile Thr Leu Ser Trp  
 450 455 460  
 Ser Gln Pro Asp Gln Pro Asn Gly Val Ile Leu Asp Tyr Glu Leu Gln  
 465 470 475 480  
 Tyr Tyr Glu Lys Asn Leu Ser Glu Leu Asn Ser Thr Ala Val Lys Ser  
 485 490 495  
 Pro Thr Asn Thr Val Thr Val Gln Asn Leu Lys Ala Gly Thr Ile Tyr  
 500 505 510  
 Val Phe Gln Val Arg Ala Arg Thr Val Ala Gly Tyr Gly Arg Tyr Ser  
 515 520 525  
 Gly Lys Met Tyr Phe Gln Thr Met Thr Glu Ala Glu Tyr Gln Thr Ser  
 530 535 540  
 Val Gln Glu Lys Leu Pro Leu Ile Ile Gly Ser Ser Ala Ala Gly Leu  
 545 550 555 560  
 Val Phe Leu Ile Ala Val Val Val Ile Ile Ile Val Cys Asn Arg Arg  
 565 570 575  
 Arg Gly Phe Glu Arg Ala Asp Ser Glu Tyr Thr Asp Lys Leu Gln His  
 580 585 590  
 Tyr Thr Ser Gly His Met Thr Pro Gly Met Lys Ile Tyr Ile Asp Pro  
 595 600 605  
 Phe Thr Tyr Glu Asp Pro Asn Glu Ala Val Arg Glu Phe Ala Lys Glu  
 610 615 620  
 Ile Asp Ile Ser Cys Val Lys Ile Glu Gln Val Ile Gly Ala Gly Glu  
 625 630 635 640

Phe Gly Glu Val Cys Ser Gly His Leu Lys Leu Pro Gly Lys Arg Glu  
 645 650 655  
 Ile Phe Val Ala Ile Lys Thr Leu Lys Ser Gly Tyr Thr Glu Lys Gln  
 660 665 670  
 Arg Arg Asp Phe Leu Ser Glu Ala Ser Ile Met Gly Gln Phe Asp His  
 675 680 685  
 Pro Asn Val Ile His Leu Glu Gly Val Val Thr Lys Ser Ser Pro Val  
 690 695 700  
 Met Ile Ile Thr Glu Phe Met Glu Asn Gly Ser Leu Asp Ser Phe Leu  
 705 710 715 720  
 Arg Gln Asn Asp Gly Gln Phe Thr Val Ile Gln Leu Val Gly Met Leu  
 725 730 735  
 Arg Gly Ile Ala Ala Gly Met Lys Tyr Leu Ala Asp Met Asn Tyr Val  
 740 745 750  
 His Arg Asp Leu Ala Ala Arg Asn Ile Leu Val Asn Ser Asn Leu Val  
 755 760 765  
 Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Phe Leu Glu Asp Asp Thr  
 770 775 780  
 Ser Asp Pro Thr Tyr Thr Ser Ala Leu Gly Gly Lys Ile Pro Ile Arg  
 785 790 795 800  
 Trp Thr Ala Pro Glu Ala Ile Gln Tyr Arg Lys Phe Thr Ser Ala Ser  
 805 810 815  
 Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met Ser Tyr Gly  
 820 825 830  
 Glu Arg Pro Tyr Trp Asp Met Thr Asn Gln Asp Val Ile Asn Ala Ile  
 835 840 845  
 Glu Gln Asp Tyr Arg Leu Pro Pro Pro Met Asp Cys Pro Asn Ala Leu  
 850 855 860  
 His Gln Leu Met Leu Asp Cys Trp Gln Lys Asp Arg Asn His Arg Pro  
 865 870 875 880  
 Lys Phe Gly Gln Ile Val Asn Thr Leu Asp Lys Met Ile Arg Asn Pro  
 885 890 895  
 Asn Ser Leu Lys Ala Met Ala Pro Leu Ser Ser Gly Val Asn Leu Pro  
 900 905 910  
 Leu Leu Asp Arg Thr Ile Pro Asp Tyr Thr Ser Phe Asn Thr Val Asp  
 915 920 925  
 Glu Trp Leu Asp Ala Ile Lys Met Ser Gln Tyr Lys Glu Ser Phe Ala  
 930 935 940  
 Ser Ala Gly Phe Thr Thr Phe Asp Ile Val Ser Gln Met Thr Val Glu  
 945 950 955 960  
 Asp Ile Leu Arg Val Gly Val Thr Leu Ala Gly His Gln Lys Lys Ile  
 965 970 975  
 Leu Asn Ser Ile Gln Val Met Arg Ala Gln Met Asn Gln Ile Gln Ser  
 980 985 990

100

Val Glu Val  
995

## (2) INFORMATION FOR SEQ ID NO:19:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 3125 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: both
- (D) TOPOLOGY: linear

## (ix) FEATURE:

- (A) NAME/KEY: CDS
- (B) LOCATION: 2..2233

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

C CTC AAA TTC ACC CTG AGG GAC TGT AAC AGC CTT CCA GGA GGA CTT	46
Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Leu Pro Gly Gly Leu	
1 5 10 15	
GGG ACT TGC AAG GAG ACT TTT AAC ATG TAC TAC TTT GAG TCA GAT GAT	94
Gly Thr Cys Lys Glu Thr Phe Asn Met Tyr Tyr Phe Glu Ser Asp Asp	
20 25 30	
GAA GAT GGG AGG AAC ATC AGA GAG AAT CAG TAC ATC AAG ATA GAT ACC	142
Glu Asp Gly Arg Asn Ile Arg Glu Asn Gln Tyr Ile Lys Ile Asp Thr	
35 40 45	
ATT GCT GCT GAT GAG AGC TTC ACG GAG TTG GAC CTC GGC GAC AGA GTT	190
Ile Ala Ala Asp Glu Ser Phe Thr Glu Leu Asp Leu Gly Asp Arg Val	
50 55 60	
ATG AAG TTA AAC ACA GAA GTG AGA GAT GTT GGG CCT CTA ACA AAA AAA	238
Met Lys Leu Asn Thr Glu Val Arg Asp Val Gly Pro Leu Thr Lys Lys	
65 70 75	
GGA TTT TAC CTT GCT TTC CAG GAT GTG GGC GCC TGC ATT GCC CTG GTC	286
Gly Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Ile Ala Leu Val	
80 85 90 95	
TCT GTG CGT GTG TAC TAC AAG AAA TGC CCA TCA GTG ATC CGC AAC CTG	334
Ser Val Arg Val Tyr Tyr Lys Lys Cys Pro Ser Val Ile Arg Asn Leu	
100 105 110	
GCA CGC TTT CCA GAT ACC ATC ACA GGA GCA GAT TCC TCG CAG CTG CTA	382
Ala Arg Phe Pro Asp Thr Ile Thr Gly Ala Asp Ser Ser Gln Leu Leu	
115 120 125	
GAA GTG TCA GGC GTC TGT GTC AAC CAC TCA GTG ACT GAT GAG GCA CCA	430
Glu Val Ser Gly Val Cys Val Asn His Ser Val Thr Asp Glu Ala Pro	
130 135 140	
AAG ATG CAC TGC AGT TCA GAG GGA GAA TGG CTG GTG CCC ATT GGG AAG	478
Lys Met His Cys Ser Ser Glu Gly Glu Trp Leu Val Pro Ile Gly Lys	
145 150 155	
TGT TTG TGC AAG GCA GGG TAC GAG GAG AAG AAC AAC ACC TGC CAA GCA	526
Cys Leu Cys Lys Ala Gly Tyr Glu Glu Lys Asn Asn Thr Cys Gln Ala	
160 165 170 175	
CCT TCT CCA GTC AGT AGT GTG AAA AAA GGG AAG ATA ACT AAA AAT AGC	574
Pro Ser Pro Val Ser Ser Val Lys Lys Gly Lys Ile Thr Lys Asn Ser	
180 185 190	

ATC Ile	TCC Ser	CTT Leu	TCC Ser	TGG Trp	CAG Gln	GAG Glu	CCA Pro	GAT Asp	CGA Arg	CCC Pro	AAC Asn	GGC Gly	ATC Ile	ATC Ile	CTG Leu	622
			195					200					205			
GAA Glu	TAC Tyr	GAA Glu	ATC Ile	AAA Lys	TAT Tyr	TTT Phe	GAA Glu	AAG Lys	GAC Asp	CAG Gln	GAG Glu	ACA Thr	AGC Ser	TAC Tyr	ACC Thr	670
		210					215					220				
ATC Ile	ATC Ile	AAA Lys	TCC Ser	AAA Lys	GAG Glu	ACC Thr	GCA Ala	ATT Ile	ACG Thr	GCA Ala	GAT Asp	GGC Gly	TTG Leu	AAA Lys	CCA Pro	718
	225					230					235					
GGC Gly	TCA Ser	GCG Ala	TAC Tyr	GTC Val	TTC Phe	CAG Gln	ATC Ile	CGA Arg	GCC Ala	CGG Arg	ACA Thr	GCT Ala	GCT Ala	GGC Gly	TAC Tyr	766
240					245					250					255	
GGT Gly	GGC Gly	TTC Phe	AGT Ser	CGA Arg	AGA Arg	TTT Phe	GAG Glu	TTT Phe	GAA Glu	ACC Thr	AGC Ser	CCA Pro	GTG Val	TTA Leu	GCT Ala	814
				260					265					270		
GCA Ala	TCC Ser	AGT Ser	GAC Asp	CAG Gln	AGC Ser	CAG Gln	ATT Ile	CCT Pro	ATA Ile	ATT Ile	GTT Val	GTG Val	TCT Ser	GTA Val	ACA Thr	862
			275					280						285		
GTG Val	GGA Gly	GTT Val	ATT Ile	CTG Leu	CTG Leu	GCT Ala	GTT Val	GTT Val	ATC Ile	GGT Gly	TTC Phe	CTT Leu	CTC Leu	AGT Ser	GGA Gly	910
		290					295					300				
AGT Ser	TGC Cys	TGC Cys	GAT Asp	CAT His	GGC Gly	TGT Cys	GGG Gly	TGG Trp	GCT Ala	TCT Ser	TCT Ser	CTG Leu	CGT Arg	GCT Ala	GTT Val	958
	305					310					315					
GCC Ala	TAT Tyr	CCG Pro	AGC Ser	CTA Leu	ATA Ile	TGG Trp	CGC Arg	TGT Cys	GGC Gly	TAC Tyr	AGC Ser	AAG Lys	GCT Ala	AAA Lys	CAA Gln	1006
	320				325					330					335	
GAC Asp	CCA Pro	GAA Glu	GAA Glu	GAA Glu	AAG Lys	ATG Met	CAT His	TTT Phe	CAT His	AAT Asn	GGC Gly	CAC His	ATT Ile	AAA Lys	CTG Leu	1054
				340					345					350		
CCT Pro	GGT Gly	GTA Val	AGA Arg	ACC Thr	TAC Tyr	ATT Ile	GAT Asp	CCC Pro	CAC His	ACC Thr	TAT Tyr	GAG Glu	GAC Asp	CCT Pro	AAT Asn	1102
			355					360					365			
CAA Gln	GCT Ala	GTC Val	CAC His	GAG Glu	TTT Phe	GCC Ala	AAG Lys	GAA Glu	ATA Ile	GAA Glu	GCT Ala	TCG Ser	TGC Cys	ATA Ile	ACC Thr	1150
		370				375						380				
ATC Ile	GAG Glu	AGA Arg	GTT Val	ATC Ile	GGA Gly	GCT Ala	GGT Gly	GAA Glu	TTT Phe	GGA Gly	GAA Glu	GTC Val	TGC Cys	AGT Ser	GGA Gly	1198
	385					390					395					
CGG Arg	CTG Leu	AAA Lys	CTG Leu	CAG Gln	GGA Gly	AAA Lys	CGC Arg	GAG Glu	TTT Phe	CCA Pro	GTG Val	GCT Ala	ATC Ile	AAA Lys	ACC Thr	1246
	400				405					410					415	
CTG Leu	AAG Lys	GTG Val	GGC Gly	TAC Tyr	ACA Thr	GAG Glu	AAG Lys	CAA Gln	AGG Arg	CGA Arg	GAT Asp	TTC Phe	CTG Leu	GGA Gly	GAA Glu	1294
				420				425					430			
GCG Ala	AGC Ser	ATC Ile	ATG Met	GGG Gly	CAG Gln	TTC Phe	GAC Asp	CAC His	CCC Pro	AAC Asn	ATC Ile	ATC Ile	CAC His	CTG Leu	GAA Glu	1342
			435				440						445			
GGT Gly	GTC Val	GTC Val	ACA Thr	AAA Lys	AGC Ser	AAA Lys	CCT Pro	GTA Val	ATG Met	ATA Ile	GTA Val	ACG Thr	GAA Glu	TAC Tyr	ATG Met	1390
		450					455					460				

102

GAA AAT GGT TCT CTG GAT ACA TTT TTA AAG AAG AAC GAT GGG CAG TTC Glu Asn Gly Ser Leu Asp Thr Phe Leu Lys Lys Asn Asp Gly Gln Phe 465 470 475	1438
ACG GTC ATT CAG CTG GTC GGG ATG CTG CGA GGC ATC GCA TCA GGG ATG Thr Val Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ser Gly Met 480 485 490 495	1486
AAG TAC CTG TCT GAC ATG GGT TAC GTA CAC AGA GAC CTC GCT GCC AGG Lys Tyr Leu Ser Asp Met Gly Tyr Val His Arg Asp Leu Ala Ala Arg 500 505 510	1534
AAT ATC CTC ATC AAC AGC AAC TTA GTC TGC AAG GTG TCT GAC TTT GGC Asn Ile Leu Ile Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly 515 520 525	1582
CTC TCC AGA GTC CTA GAA GAT GAT CCT GAA GCA GCG TAC ACA ACC AGG Leu Ser Arg Val Leu Glu Asp Asp Pro Glu Ala Ala Tyr Thr Thr Arg 530 535 540	1630
GGA GGG AAG ATC CCC ATC CGA TGG ACG GCA CCT GAA GCA ATC GCC TTC Gly Gly Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Ala Phe 545 550 555	1678
CGC AAA TTC ACG TCG GCC AGC GAT GTG TGG AGC TAC GGC ATT GTG ATG Arg Lys Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Met 560 565 570 575	1726
TGG GAA GTG ATG TCC TAT GGC GAG AGA CCT TAC TGG GAA ATG ACA AAC Trp Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Glu Met Thr Asn 580 585 590	1774
CAA GAT GTG ATT AAA GCC GTG GAG GAA GGC TAT CGC CTG CCA AGT CCC Gln Asp Val Ile Lys Ala Val Glu Glu Gly Tyr Arg Leu Pro Ser Pro 595 600 605	1822
ATG GAC TGC CCT GCT GCT CTC TAC CAG TTG ATG CTT GAC TGC TGG CAG Met Asp Cys Pro Ala Ala Leu Tyr Gln Leu Met Leu Asp Cys Trp Gln 610 615 620	1870
AAA GAC CGC AAC AGC AGG CCC AAG TTT GAT GAA ATT GTC AGC ATG TTG Lys Asp Arg Asn Ser Arg Pro Lys Phe Asp Glu Ile Val Ser Met Leu 625 630 635	1918
GAC AAG CTC ATC CGT AAC CCA AGC AGC TTG AAG ACG TTG GTT AAT GCA Asp Lys Leu Ile Arg Asn Pro Ser Ser Leu Lys Thr Leu Val Asn Ala 640 645 650 655	1966
TCG AGC AGA GTA TCA AAT TTG TTG GTA GAA CAC AGT CCA GTG GGG AGC Ser Ser Arg Val Ser Asn Leu Leu Val Glu His Ser Pro Val Gly Ser 660 665 670	2014
GGT GCC TAC AGG TCA GTG GGT GAG TGG CTG GAA GCC ATC AAA ATG GGT Gly Ala Tyr Arg Ser Val Gly Glu Trp Leu Glu Ala Ile Lys Met Gly 675 680 685	2062
CGA TAC ACC GAG ATT TTC ATG GAG AAT GGA TAC AGT TCG ATG GAT TCT Arg Tyr Thr Glu Ile Phe Met Glu Asn Gly Tyr Ser Ser Met Asp Ser 690 695 700	2110
GTG GCT CAG GTG ACC CTA GAG GAT TTG AGG CGG CTG GGA GTG ACA CTT Val Ala Gln Val Thr Leu Glu Asp Leu Arg Arg Leu Gly Val Thr Leu 705 710 715	2158
GTT GGT CAC CAG AAG AAG ATA ATG AAC AGC CTT CAA GAG ATG AAG GTC Val Gly His Gln Lys Lys Ile Met Asn Ser Leu Gln Glu Met Lys Val 720 725 730 735	2206



103

CAG TTG GTG AAT GGG ATG GTG CCA TTG TAACTCGGTT TTTAAGTCAC 2253  
 Gln Leu Val Asn Gly Met Val Pro Leu  
 740

TTCCTCGAGT GGTCGGTCCT GCACTTTGTA TACTAGCTCT GAGATTTATT TTGACTAAAG 2313  
 AAGAAAAAAG GGAAATTCAG TGGTTTCTGT AACTGAAGGA CGCTGGCTTC TGCCACAGCA 2373  
 TTTATAAAGC AGTGTTTGAC TGAAGTTTTC ATTTTCTTCC TATTTGTGTC CTCATTCTCA 2433  
 TGAAGTAAAT GTAACATGCA TGGAACATGG AAATGGATCT ACTGTACATG AGGTTACCCA 2493  
 ATTTCTTGCG CTTCAGCATG ACAACAGCAA GCCTTCCCAC CACATGTTGT CTATACATGG 2553  
 GAGATATATA TATATGCATA TATATATATA GCACCTTTAT ATACTGAATT ACAGCAGCAG 2613  
 CACATGTTAA TACTTCCAAG GACTTACTTG ACTAGAGAAG TTTTGCAGCC ATTGTGGGCT 2673  
 CACACAAGCT GCGGTTTACT GAAGTTTACT TCAAGTCTTA CTTGTCTACA GAAGTGATT 2733  
 GAAGAGCAAT ATGATTAGAT TATTTCTGGA TAGATATTTT GTTTTGTAAG TTTAAAAAAT 2793  
 CGTGTTACAC AGCGTTAAGT TATAGAGACT AGTGATATAA CATGTTGCTT GCTCAATGGC 2853  
 AAATACAATA CAGGGTGTAT ATTTTTTTCT CTCTGTGTTG CAAAGTTCTT TTAGTTTGCT 2913  
 CTTCTGTGAG GATAATACGT TATGATGTAT ATACTGTACA GTTTGCTACA CATCAGGTAC 2973  
 AAGATTGGGG CTTTCTCAAT GTTTGTTCT TTTCCCTCT TTTGTTTCAT TTTGTCTTCC 3033  
 TTTTGTGTTA ACCACTATGC TTTGTATTTT TGCTGCTGTT TGGTTTGAGG CAACATATAA 3093  
 AGCTTTCAGG TGTTTTGATT ATAAAAAAA AG 3125

## (2) INFORMATION FOR SEQ ID NO:20:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 744 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: protein

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Leu Pro Gly Gly Leu Gly  
 1 5 10 15

Thr Cys Lys Glu Thr Phe Asn Met Tyr Tyr Phe Glu Ser Asp Asp Glu  
 20 25 30

Asp Gly Arg Asn Ile Arg Glu Asn Gln Tyr Ile Lys Ile Asp Thr Ile  
 35 40 45

Ala Ala Asp Glu Ser Phe Thr Glu Leu Asp Leu Gly Asp Arg Val Met  
 50 55 60

Lys Leu Asn Thr Glu Val Arg Asp Val Gly Pro Leu Thr Lys Lys Gly  
 65 70 75 80

Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Ile Ala Leu Val Ser  
 85 90 95

Val Arg Val Tyr Tyr Lys Lys Cys Pro Ser Val Ile Arg Asn Leu Ala  
 100 105 110

104

Arg	Phe	Pro	Asp	Thr	Ile	Thr	Gly	Ala	Asp	Ser	Ser	Gln	Leu	Leu	Glu
		115					120					125			
Val	Ser	Gly	Val	Cys	Val	Asn	His	Ser	Val	Thr	Asp	Glu	Ala	Pro	Lys
	130					135					140				
Met	His	Cys	Ser	Ser	Glu	Gly	Glu	Trp	Leu	Val	Pro	Ile	Gly	Lys	Cys
145					150					155					160
Leu	Cys	Lys	Ala	Gly	Tyr	Glu	Glu	Lys	Asn	Asn	Thr	Cys	Gln	Ala	Pro
				165					170					175	
Ser	Pro	Val	Ser	Ser	Val	Lys	Lys	Gly	Lys	Ile	Thr	Lys	Asn	Ser	Ile
			180					185					190		
Ser	Leu	Ser	Trp	Gln	Glu	Pro	Asp	Arg	Pro	Asn	Gly	Ile	Ile	Leu	Glu
		195					200					205			
Tyr	Glu	Ile	Lys	Tyr	Phe	Glu	Lys	Asp	Gln	Glu	Thr	Ser	Tyr	Thr	Ile
	210					215					220				
Ile	Lys	Ser	Lys	Glu	Thr	Ala	Ile	Thr	Ala	Asp	Gly	Leu	Lys	Pro	Gly
225					230					235					240
Ser	Ala	Tyr	Val	Phe	Gln	Ile	Arg	Ala	Arg	Thr	Ala	Ala	Gly	Tyr	Gly
				245					250					255	
Gly	Phe	Ser	Arg	Arg	Phe	Glu	Phe	Glu	Thr	Ser	Pro	Val	Leu	Ala	Ala
			260					265					270		
Ser	Ser	Asp	Gln	Ser	Gln	Ile	Pro	Ile	Ile	Val	Val	Ser	Val	Thr	Val
		275					280					285			
Gly	Val	Ile	Leu	Leu	Ala	Val	Val	Ile	Gly	Phe	Leu	Leu	Ser	Gly	Ser
	290					295					300				
Cys	Cys	Asp	His	Gly	Cys	Gly	Trp	Ala	Ser	Ser	Leu	Arg	Ala	Val	Ala
305					310					315					320
Tyr	Pro	Ser	Leu	Ile	Trp	Arg	Cys	Gly	Tyr	Ser	Lys	Ala	Lys	Gln	Asp
				325					330					335	
Pro	Glu	Glu	Glu	Lys	Met	His	Phe	His	Asn	Gly	His	Ile	Lys	Leu	Pro
			340					345					350		
Gly	Val	Arg	Thr	Tyr	Ile	Asp	Pro	His	Thr	Tyr	Glu	Asp	Pro	Asn	Gln
		355					360					365			
Ala	Val	His	Glu	Phe	Ala	Lys	Glu	Ile	Glu	Ala	Ser	Cys	Ile	Thr	Ile
	370					375					380				
Glu	Arg	Val	Ile	Gly	Ala	Gly	Glu	Phe	Gly	Glu	Val	Cys	Ser	Gly	Arg
385					390					395					400
Leu	Lys	Leu	Gln	Gly	Lys	Arg	Glu	Phe	Pro	Val	Ala	Ile	Lys	Thr	Leu
				405					410					415	
Lys	Val	Gly	Tyr	Thr	Glu	Lys	Gln	Arg	Arg	Asp	Phe	Leu	Gly	Glu	Ala
			420					425					430		
Ser	Ile	Met	Gly	Gln	Phe	Asp	His	Pro	Asn	Ile	Ile	His	Leu	Glu	Gly
		435					440					445			
Val	Val	Thr	Lys	Ser	Lys	Pro	Val	Met	Ile	Val	Thr	Glu	Tyr	Met	Glu
	450					455					460				

105

Asn Gly Ser Leu Asp Thr Phe Leu Lys Lys Asn Asp Gly Gln Phe Thr  
 465 470 475 480  
 Val Ile Gln Leu Val Gly Met Leu Arg Gly Ile Ala Ser Gly Met Lys  
 485 490 495  
 Tyr Leu Ser Asp Met Gly Tyr Val His Arg Asp Leu Ala Ala Arg Asn  
 500 505 510  
 Ile Leu Ile Asn Ser Asn Leu Val Cys Lys Val Ser Asp Phe Gly Leu  
 515 520 525  
 Ser Arg Val Leu Glu Asp Asp Pro Glu Ala Ala Tyr Thr Thr Arg Gly  
 530 535 540  
 Gly Lys Ile Pro Ile Arg Trp Thr Ala Pro Glu Ala Ile Ala Phe Arg  
 545 550 555 560  
 Lys Phe Thr Ser Ala Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp  
 565 570 575  
 Glu Val Met Ser Tyr Gly Glu Arg Pro Tyr Trp Glu Met Thr Asn Gln  
 580 585 590  
 Asp Val Ile Lys Ala Val Glu Glu Gly Tyr Arg Leu Pro Ser Pro Met  
 595 600 605  
 Asp Cys Pro Ala Ala Leu Tyr Gln Leu Met Leu Asp Cys Trp Gln Lys  
 610 615 620  
 Asp Arg Asn Ser Arg Pro Lys Phe Asp Glu Ile Val Ser Met Leu Asp  
 625 630 635 640  
 Lys Leu Ile Arg Asn Pro Ser Ser Leu Lys Thr Leu Val Asn Ala Ser  
 645 650 655  
 Ser Arg Val Ser Asn Leu Leu Val Glu His Ser Pro Val Gly Ser Gly  
 660 665 670  
 Ala Tyr Arg Ser Val Gly Glu Trp Leu Glu Ala Ile Lys Met Gly Arg  
 675 680 685  
 Tyr Thr Glu Ile Phe Met Glu Asn Gly Tyr Ser Ser Met Asp Ser Val  
 690 695 700  
 Ala Gln Val Thr Leu Glu Asp Leu Arg Arg Leu Gly Val Thr Leu Val  
 705 710 715 720  
 Gly His Gln Lys Lys Ile Met Asn Ser Leu Gln Glu Met Lys Val Gln  
 725 730 735  
 Leu Val Asn Gly Met Val Pro Leu  
 740

## (2) INFORMATION FOR SEQ ID NO:21:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 3056 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: both
  - (D) TOPOLOGY: linear

106

## (ix) FEATURE:

(A) NAME/KEY: CDS

(B) LOCATION: 2..2131

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

C CTC AAA TTC ACC CTG AGG GAC TGT AAC AGC CTT CCA GGA GGA CTT	46
Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Leu Pro Gly Gly Leu	
1 5 10 15	
GGG ACT TGC AAG GAG ACT TTT AAC ATG TAC TAC TTT GAG TCA GAT GAT	94
Gly Thr Cys Lys Glu Thr Phe Asn Met Tyr Tyr Phe Glu Ser Asp Asp	
20 25 30	
GAA GAT GGG AGG AAC ATC AGA GAG AAT CAG TAC ATC AAG ATA GAT ACC	142
Glu Asp Gly Arg Asn Ile Arg Glu Asn Gln Tyr Ile Lys Ile Asp Thr	
35 40 45	
ATT GCT GCT GAT GAG AGC TTC ACG GAG TTG GAC CTC GGC GAC AGA GTT	190
Ile Ala Ala Asp Glu Ser Phe Thr Glu Leu Asp Leu Gly Asp Arg Val	
50 55 60	
ATG AAG TTA AAC ACA GAA GTG AGA GAT GTT GGG CCT CTA ACA AAA AAA	238
Met Lys Leu Asn Thr Glu Val Arg Asp Val Gly Pro Leu Thr Lys Lys	
65 70 75	
GGA TTT TAC CTT GCT TTC CAG GAT GTG GGC GCC TGC ATT GCC CTG GTC	286
Gly Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Ile Ala Leu Val	
80 85 90 95	
TCT GTG CGT GTG TAC TAC AAG AAA TGC CCA TCA GTG ATC CGC AAC CTG	334
Ser Val Arg Val Tyr Tyr Lys Lys Cys Pro Ser Val Ile Arg Asn Leu	
100 105 110	
GCA CGC TTT CCA GAT ACC ATC ACA GGA GCA GAT TCC TCG CAG CTG CTA	382
Ala Arg Phe Pro Asp Thr Ile Thr Gly Ala Asp Ser Ser Gln Leu Leu	
115 120 125	
GAA GTG TCA GGC GTC TGT GTC AAC CAC TCA GTG ACT GAT GAG GCA CCA	430
Glu Val Ser Gly Val Cys Val Asn His Ser Val Thr Asp Glu Ala Pro	
130 135 140	
AAG ATG CAC TGC AGT TCA GAG GGA GAA TGG CTG GTG CCC ATT GGG AAG	478
Lys Met His Cys Ser Ser Glu Gly Glu Trp Leu Val Pro Ile Gly Lys	
145 150 155	
TGT TTG TGC AAG GCA GGG TAC GAG GAG AAG AAC AAC ACC TGC CAA GCA	526
Cys Leu Cys Lys Ala Gly Tyr Glu Glu Lys Asn Asn Thr Cys Gln Ala	
160 165 170 175	
CCT TCT CCA GTC AGT AGT GTG AAA AAA GGG AAG ATA ACT AAA AAT AGC	574
Pro Ser Pro Val Ser Ser Val Lys Lys Gly Lys Ile Thr Lys Asn Ser	
180 185 190	
ATC TCC CTT TCC TGG CAG GAG CCA GAT CGA CCC AAC GGC ATC ATC CTG	622
Ile Ser Leu Ser Trp Gln Glu Pro Asp Arg Pro Asn Gly Ile Ile Leu	
195 200 205	
GAA TAC GAA ATC AAA TAT TTT GAA AAG GAC CAG GAG ACA AGC TAC ACC	670
Glu Tyr Glu Ile Lys Tyr Phe Glu Lys Asp Gln Glu Thr Ser Tyr Thr	
210 215 220	
ATC ATC AAA TCC AAA GAG ACC GCA ATT ACG GCA GAT GGC TTG AAA CCA	718
Ile Ile Lys Ser Lys Glu Thr Ala Ile Thr Ala Asp Gly Leu Lys Pro	
225 230 235	

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GGC 240	TCA Ser	GCG Ala	TAC Tyr	GTC Val	TTC Phe	CAG Gln	ATC Ile	CGA Arg	GCC Ala	CGG Arg	ACA Thr	GCT Ala	GCT Ala	GGC Gly	TAC Tyr	766
GGT Gly	GGC Gly	TTC Phe	AGT Ser	CGA Arg	AGA Arg	TTT Phe	GAG Glu	TTT Phe	GAA Glu	ACC Thr	AGC Ser	CCA Pro	GTG Val	TTA Leu	GCT Ala	814
GCA Ala	TCC Ser	AGT Ser	GAC Asp	CAG Gln	AGC Ser	CAG Gln	ATT Ile	CCT Pro	ATA Ile	ATT Ile	GTT Val	GTG Val	TCT Val	GTA Val	ACA Thr	862
GTG Val	GGA Gly	GTT Val	ATT Ile	CTG Leu	CTG Leu	GCT Ala	GTT Val	GTT Val	ATC Ile	GGT Gly	TTC Phe	CTT Leu	CTC Leu	AGT Ser	GGA Gly	910
AGG Arg	CGC Arg	TGT Cys	GGC Gly	TAC Tyr	AGC Ser	AAG Lys	GCT Ala	AAA Lys	CAA Gln	GAC Asp	CCA Pro	GAA Glu	GAA Glu	GAA Glu	AAG Lys	958
ATG 320	CAT His	TTT Phe	CAT His	AAT Asn	GGC Gly	CAC His	ATT Ile	AAA Lys	CTG Leu	CCT Pro	GGT Gly	GTA Val	AGA Arg	ACC Thr	TAC Tyr	1006
ATT Ile	GAT Asp	CCC Pro	CAC His	ACC Thr	TAT Tyr	GAG Glu	GAC Asp	CCT Pro	AAT Asn	CAA Gln	GCT Ala	GTC Val	CAC His	GAG Glu	TTT Phe	1054
GCC Ala	AAG Lys	GAA Glu	ATA Ile	GAA Glu	GCT Ala	TCG Ser	TGC Cys	ATA Ile	ACC Thr	ATC Ile	GAG Glu	AGA Arg	GTT Val	ATC Ile	GGA Gly	1102
GCT Ala	GGT Gly	GAA Glu	TTT Phe	GGA Gly	GAA Glu	GTC Val	TGC Cys	AGT Ser	GGA Gly	CGG Arg	CTG Leu	AAA Lys	CTG Leu	CAG Gln	GGA Gly	1150
AAA Lys	CGC Arg	GAG Glu	TTT Phe	CCA Pro	GTG Val	GCT Ala	ATC Ile	AAA Lys	ACC Thr	CTG Leu	AAG Lys	GTG Val	GGC Gly	TAC Tyr	ACA Thr	1198
GAG 400	AAG Lys	CAA Gln	AGG Arg	CGA Arg	GAT Asp	TTC Phe	CTG Leu	GGA Gly	GAA Glu	GCG Ala	AGC Ser	ATC Ile	ATG Met	GGG Gly	CAG Gln	1246
TTC Phe	GAC Asp	CAC His	CCC Pro	AAC Asn	ATC Ile	ATC Ile	CAC His	CTG Leu	GAA Glu	GGT Gly	GTC Val	GTC Val	ACA Thr	AAA Lys	AGC Ser	1294
AAA Lys	CCT Pro	GTA Val	ATG Met	ATA Ile	GTA Val	ACG Thr	GAA Glu	TAC Tyr	ATG Met	GAA Glu	AAT Asn	GGT Gly	TCT Ser	CTG Leu	GAT Asp	1342
ACA Thr	TTT Phe	TTA Leu	AAG Lys	AAG Lys	AAC Asn	GAT Asp	GGG Gly	CAG Gln	TTC Phe	ACG Thr	GTC Val	ATT Ile	CAG Gln	CTG Leu	GTC Val	1390
GGG Gly	ATG Met	CTG Leu	CGA Arg	GGC Gly	ATC Ile	GCA Ala	TCA Ser	GGG Gly	ATG Met	AAG Lys	TAC Tyr	CTG Leu	TCT Ser	GAC Asp	ATG Met	1438
GGT 480	TAC Tyr	GTA Val	CAC His	AGA Arg	GAC Asp	CTC Leu	GCT Ala	GCC Ala	AGG Arg	AAT Asn	ATC Ile	CTC Leu	ATC Ile	AAC Asn	AGC Ser	1486
AAC Asn	TTA Leu	GTC Val	TGC Cys	AAG Lys	GTG Val	TCT Ser	GAC Asp	TTT Phe	GGC Gly	CTC Leu	TCC Ser	AGA Arg	GTC Val	CTA Leu	GAA Glu	1534

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GAT GAT CCT GAA GCA GCG TAC ACA ACC AGG GGA GGG AAG ATC CCC ATC Asp Asp Pro Glu Ala Ala Tyr Thr Thr Arg Gly Gly Lys Ile Pro Ile 515 520 525	1582
CGA TGG ACG GCA CCT GAA GCA ATC GCC TTC CGC AAA TTC ACG TCG GCC Arg Trp Thr Ala Pro Glu Ala Ile Ala Phe Arg Lys Phe Thr Ser Ala 530 535 540	1630
AGC GAT GTG TGG AGC TAC GGC ATT GTG ATG TGG GAA GTG ATG TCC TAT Ser Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met Ser Tyr 545 550 555	1678
GGC GAG AGA CCT TAC TGG GAA ATG ACA AAC CAA GAT GTG ATT AAA GCC Gly Glu Arg Pro Tyr Trp Glu Met Thr Asn Gln Asp Val Ile Lys Ala 560 565 570 575	1726
GTG GAG GAA GGC TAT CGC CTG CCA AGT CCC ATG GAC TGC CCT GCT GCT Val Glu Glu Gly Tyr Arg Leu Pro Ser Pro Met Asp Cys Pro Ala Ala 580 585 590	1774
CTC TAC CAG TTG ATG CTT GAC TGC TGG CAG AAA GAC CGC AAC AGC AGG Leu Tyr Gln Leu Met Leu Asp Cys Trp Gln Lys Asp Arg Asn Ser Arg 595 600 605	1822
CCC AAG TTT GAT GAA ATT GTC AGC ATG TTG GAC AAG CTC ATC CGT AAC Pro Lys Phe Asp Glu Ile Val Ser Met Leu Asp Lys Leu Ile Arg Asn 610 615 620	1870
CCA AGC AGC TTG AAG ACG TTG GTT AAT GCA TCG AGC AGA GTA TCA AAT Pro Ser Ser Leu Lys Thr Leu Val Asn Ala Ser Ser Arg Val Ser Asn 625 630 635	1918
TTG TTG GTA GAA CAC AGT CCA GTG GGG AGC GGT GCC TAC AGG TCA GTG Leu Leu Val Glu His Ser Pro Val Gly Ser Gly Ala Tyr Arg Ser Val 640 645 650 655	1966
GGT GAG TGG CTG GAA GCC ATC AAA ATG GGT CGA TAC ACC GAG ATT TTC Gly Glu Trp Leu Glu Ala Ile Lys Met Gly Arg Tyr Thr Glu Ile Phe 660 665 670	2014
ATG GAG AAT GGA TAC AGT TCG ATG GAT TCT GTG GCT CAG GTG ACC CTA Met Glu Asn Gly Tyr Ser Ser Met Asp Ser Val Ala Gln Val Thr Leu 675 680 685	2062
GAG GAC GAA TCA CCT TGT GAA AAG TGG AGC CTC ACC CTC CAC CCC CTC Glu Asp Glu Ser Pro Cys Glu Lys Trp Ser Leu Thr Leu His Pro Leu 690 695 700	2110
TTT CCA ACT GGA TAT CAG ACT TGAAGGAAAC CTTTCCAGTG GACCAGACCT Phe Pro Thr Gly Tyr Gln Thr 705 710	2161
GCTCTTTAAA CTTGTGGACC ACCTAGTGAC TTTGAGTGTG TCTGGAGCTC TTTCAATCCA	2221
CTGCAAGAAT AACTTTACCA GGACAGTACT CAAGAATAGA TAGATCCATG ACATGAGTTT	2281
CAGTCTGATA TTTGACTGGA CCAATTACTA ACAAATGTG GACTGCATAC TTACACCTTT	2341
TGAAAGATCT GTACTCACCG AATCTCAGGA CACCCTGTTG TTTGTTATTA GATGAAGAAC	2401
TCTGAATATT TGTAATAATA TGTGATGTGT TGCTTTGCAT TGTATTTTTT TCTTATAAAA	2461
TAAAATAAAT TATTTATTAA AAGTTATACT GGGATGAAGA CCATTTAAGA GTTCACCTGC	2521
TCTAGATGCT TATTCCTAAC CTGAAACCTC AGTTCCGGAT AGTGATACTG CACACGCTTG	2581
TGAACAAACC CATTCTCGTG TCATAACCAA ACAGGATGGG AGTAATGAAT AAGAGCAGAT	2641

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GAACTCTTAA AAGAAAGATC CTAATCTCAT GCAAAGGTCC CTTGCAAGTG GATTCCTCTC 2701  
 TCCCTAGCGT CTTCTAAAGG TCTTTGAGGT TATTCTTTCC CCTCTTTCAA ACTGACAGCT 2761  
 AACTCTGTGA GTAGTGTGAG TCTGCATGGG CCAGTGTAGA ACTGCACCAT GTTGAAGAAG 2821  
 AGTGCTGCAA TATGGCTGGG GTGGGAGATG AAATGCAAAG TAATCTCTGG TAGGCTGATG 2881  
 GCTTCCAGCC ATGGAGGTAT TTCAGGAACC TGGCCCTTTT GCTTGCATGA GTAATGAATG 2941  
 GAGTGGTGAG GAGTGTGTGA TTTTATGTGG CAATCCAGTC CTAGTCTACA CTGTGTTTGA 3001  
 CAAATTGGTC CATGGTGTAT AAGTAGTTCT ATTTGTAAAT AAAATGTTTT AAATG 3056

## (2) INFORMATION FOR SEQ ID NO:22:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 710 amino acids  
 (B) TYPE: amino acid  
 (D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: protein

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

Leu Lys Phe Thr Leu Arg Asp Cys Asn Ser Leu Pro Gly Gly Leu Gly  
 1 5 10 15  
 Thr Cys Lys Glu Thr Phe Asn Met Tyr Tyr Phe Glu Ser Asp Asp Glu  
 20 25 30  
 Asp Gly Arg Asn Ile Arg Glu Asn Gln Tyr Ile Lys Ile Asp Thr Ile  
 35 40 45  
 Ala Ala Asp Glu Ser Phe Thr Glu Leu Asp Leu Gly Asp Arg Val Met  
 50 55 60  
 Lys Leu Asn Thr Glu Val Arg Asp Val Gly Pro Leu Thr Lys Lys Gly  
 65 70 75 80  
 Phe Tyr Leu Ala Phe Gln Asp Val Gly Ala Cys Ile Ala Leu Val Ser  
 85 90 95  
 Val Arg Val Tyr Tyr Lys Lys Cys Pro Ser Val Ile Arg Asn Leu Ala  
 100 105 110  
 Arg Phe Pro Asp Thr Ile Thr Gly Ala Asp Ser Ser Gln Leu Leu Glu  
 115 120 125  
 Val Ser Gly Val Cys Val Asn His Ser Val Thr Asp Glu Ala Pro Lys  
 130 135 140  
 Met His Cys Ser Ser Glu Gly Glu Trp Leu Val Pro Ile Gly Lys Cys  
 145 150 155 160  
 Leu Cys Lys Ala Gly Tyr Glu Glu Lys Asn Asn Thr Cys Gln Ala Pro  
 165 170 175  
 Ser Pro Val Ser Ser Val Lys Lys Gly Lys Ile Thr Lys Asn Ser Ile  
 180 185 190  
 Ser Leu Ser Trp Gln Glu Pro Asp Arg Pro Asn Gly Ile Ile Leu Glu  
 195 200 205  
 Tyr Glu Ile Lys Tyr Phe Glu Lys Asp Gln Glu Thr Ser Tyr Thr Ile  
 210 215 220

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Ile Lys Ser Lys Glu Thr Ala Ile Thr Ala Asp Gly Leu Lys Pro Gly  
 225 230 235 240  
 Ser Ala Tyr Val Phe Gln Ile Arg Ala Arg Thr Ala Ala Gly Tyr Gly  
 245 250 255  
 Gly Phe Ser Arg Arg Phe Glu Phe Glu Thr Ser Pro Val Leu Ala Ala  
 260 265 270  
 Ser Ser Asp Gln Ser Gln Ile Pro Ile Ile Val Val Ser Val Thr Val  
 275 280 285  
 Gly Val Ile Leu Leu Ala Val Val Ile Gly Phe Leu Leu Ser Gly Arg  
 290 295 300  
 Arg Cys Gly Tyr Ser Lys Ala Lys Gln Asp Pro Glu Glu Glu Lys Met  
 305 310 315 320  
 His Phe His Asn Gly His Ile Lys Leu Pro Gly Val Arg Thr Tyr Ile  
 325 330 335  
 Asp Pro His Thr Tyr Glu Asp Pro Asn Gln Ala Val His Glu Phe Ala  
 340 345 350  
 Lys Glu Ile Glu Ala Ser Cys Ile Thr Ile Glu Arg Val Ile Gly Ala  
 355 360 365  
 Gly Glu Phe Gly Glu Val Cys Ser Gly Arg Leu Lys Leu Gln Gly Lys  
 370 375 380  
 Arg Glu Phe Pro Val Ala Ile Lys Thr Leu Lys Val Gly Tyr Thr Glu  
 385 390 395 400  
 Lys Gln Arg Arg Asp Phe Leu Gly Glu Ala Ser Ile Met Gly Gln Phe  
 405 410 415  
 Asp His Pro Asn Ile Ile His Leu Glu Gly Val Val Thr Lys Ser Lys  
 420 425 430  
 Pro Val Met Ile Val Thr Glu Tyr Met Glu Asn Gly Ser Leu Asp Thr  
 435 440 445  
 Phe Leu Lys Lys Asn Asp Gly Gln Phe Thr Val Ile Gln Leu Val Gly  
 450 455 460  
 Met Leu Arg Gly Ile Ala Ser Gly Met Lys Tyr Leu Ser Asp Met Gly  
 465 470 475 480  
 Tyr Val His Arg Asp Leu Ala Ala Arg Asn Ile Leu Ile Asn Ser Asn  
 485 490 495  
 Leu Val Cys Lys Val Ser Asp Phe Gly Leu Ser Arg Val Leu Glu Asp  
 500 505 510  
 Asp Pro Glu Ala Ala Tyr Thr Thr Arg Gly Gly Lys Ile Pro Ile Arg  
 515 520 525  
 Trp Thr Ala Pro Glu Ala Ile Ala Phe Arg Lys Phe Thr Ser Ala Ser  
 530 535 540  
 Asp Val Trp Ser Tyr Gly Ile Val Met Trp Glu Val Met Ser Tyr Gly  
 545 550 555 560  
 Glu Arg Pro Tyr Trp Glu Met Thr Asn Gln Asp Val Ile Lys Ala Val  
 565 570 575



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Glu Glu Gly Tyr Arg Leu Pro Ser Pro Met Asp Cys Pro Ala Ala Leu  
                   580                                  585                                  590  
 Tyr Gln Leu Met Leu Asp Cys Trp Gln Lys Asp Arg Asn Ser Arg Pro  
                   595                                  600                                  605  
 Lys Phe Asp Glu Ile Val Ser Met Leu Asp Lys Leu Ile Arg Asn Pro  
                   610                                  615                                  620  
 Ser Ser Leu Lys Thr Leu Val Asn Ala Ser Ser Arg Val Ser Asn Leu  
                   625                                  630                                  635                                  640  
 Leu Val Glu His Ser Pro Val Gly Ser Gly Ala Tyr Arg Ser Val Gly  
                                   645                                  650                                  655  
 Glu Trp Leu Glu Ala Ile Lys Met Gly Arg Tyr Thr Glu Ile Phe Met  
                                   660                                  665                                  670  
 Glu Asn Gly Tyr Ser Ser Met Asp Ser Val Ala Gln Val Thr Leu Glu  
                   675                                  680                                  685  
 Asp Glu Ser Pro Cys Glu Lys Trp Ser Leu Thr Leu His Pro Leu Phe  
                   690                                  695                                  700  
 Pro Thr Gly Tyr Gln Thr  
                   705                                  710

## (2) INFORMATION FOR SEQ ID NO:23:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 19 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

Arg Ile Cys Thr Pro Asp Val Ser Gly Thr Val Gly Ser Arg Pro Ala  
 1                  5                                  10                                  15  
 Ala Asp His

## (2) INFORMATION FOR SEQ ID NO:24:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 13 amino acids
  - (B) TYPE: amino acid
  - (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

Cys Leu Glu Thr His Thr Lys Asn Ser Pro Val Pro Val  
 1                                  5                                  10

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## (2) INFORMATION FOR SEQ ID NO:25:

- (i) SEQUENCE CHARACTERISTICS:  
    (A) LENGTH: 12 amino acids  
    (B) TYPE: amino acid  
    (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

Lys Met Gln Gln Met His Gly Arg Met Val Pro Val  
1                    5                    10

## (2) INFORMATION FOR SEQ ID NO:26:

- (i) SEQUENCE CHARACTERISTICS:  
    (A) LENGTH: 12 amino acids  
    (B) TYPE: amino acid  
    (D) TOPOLOGY: linear

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

Lys Val His Leu Asn Gln Leu Glu Pro Val Glu Val  
1                    5                    10

What is claimed is:

1. A composition of matter, comprising an isolated nucleic acid sequence encoding a Eph-related protein tyrosine kinase, or functional fragment thereof, having about 23 to 66 percent amino acid sequence identity  
5 in its carboxyl terminal variable region compared to known members of the Eph subclass of tyrosine kinases.
  2. The composition of claim 1, comprising substantially the same nucleotide sequence selected from the group consisting of SEQ ID NOS: 3, 7, 9, 11, 13, 19 and  
10 21.
  3. A composition of matter, comprising a vector containing the nucleic acid of claim 1.
  4. The composition of claim 3, wherein said vector is for the expression of a recombinant Eph-related  
15 protein tyrosine kinase.
  5. The composition of claim 4, wherein said expression is in a procaryotic host.
  6. The composition of claim 4, wherein said expression is in a eucaryotic host.
  - 20 7. A composition of matter, comprising a host cell containing the vector of claim 3.
  8. The composition of claim 7, wherein said host cell is procaryotic.
  9. The composition of claim 7, wherein said  
25 host cell is eucaryotic.
-

10. A composition of matter, comprising a substantially purified Eph-related protein tyrosine kinase, or functional fragment thereof, having about 23 to 66 percent amino acid sequence identity in its carboxyl terminal variable region compared to known members of the Eph subclass of tyrosine kinases.

11. The composition of claim 10, comprising substantially the same amino acid sequence selected from the group consisting of SEQ ID NOS: 4, 8, 10, 12, 14, 20 and 22.

12. A composition of matter, comprising a substantially purified chicken Eph-related protein tyrosine kinase, or functional fragment thereof having substantially the same amino acid sequence of SEQ ID NO: 2.

13. A composition of matter, comprising a substantially purified chicken Eph-related protein tyrosine kinase, or functional fragment thereof having substantially the same amino acid sequence of SEQ ID NO: 6.

14. A method of diagnosing cancer, comprising removing a tissue or cell sample from a subject suspected of having cancer and determining the level of Eph-related protein tyrosine kinase in said sample, wherein a change in the level or activity of a Eph-related protein tyrosine kinase compared to a normal sample indicates the presence of a cancer or correlates with a specific prognosis.

15. The method of claim 13, wherein an increase in said change in the level or activity of a Eph-related protein tyrosine kinase indicates the presence of a cancer or correlates with a specific prognosis.

16. The method of claim 13, wherein a decrease in said change in the level or activity of a Eph-related protein tyrosine kinase indicates the presence of a cancer or correlates with a specific prognosis.

- 5           17. The method of claim 12, wherein said cancer is selected from the group consisting of liver carcinoma, lung carcinoma, breast carcinoma, colon carcinoma and leukemia.

1 MPGPRTMGPIWFCIPIALPLLAVEETIMDSTTATAELGMVHP-PSGWEVSGYDENMTIRTYQVCNVFE-SSQNNWLRTKYIRRR-GAHRH  
 1 GVSSRRARPPGSSRSRRGV.S.A.TT.-ET.....A.QP.....Q.R.-AQ.QQ.....F.N.Q-DVQ.VY  
 1 .....TR.....TAN.-.....L.....-PN.....L.TF.N.....Y  
 1 .DRRRRLPLL.CAALGSAGR.SARPGN.VN.L.K.IQG.....ISY.-SH.....I.V.HYTP.....ES..MD-H.....NW.P.N-S.QK.Y  
 1 MELOARACEAL..G.--A..AAAAQK.VV.L.FAA.GG.....LT..YK..DLMQIMND.-P.YM.S.....MS-GD.D.....NWVY.G-E.E.NN  
 1 MERRW.LGIGIV.LL.---AP.P.GAR.K.V....TSK.QG....LLD.PKD..S.OOOILNGT-PLYM.D.PMQGRDTHD.....SNW.Y.GEE.S.V.

96 VEMKFSVRDCSSIPNVP--SCKETFNLYYESDFDSATKTFPNMNMENPMKVDTIAADESFSQVDLGGRMKINTEVRSFGPVSXNGFYLAFOYGGCM  
 79 ..L..T....K..KI..---.....F.....T....SANS.F.....YI.....P.....KLES.-.....K.....L.....L.A..  
 68 T..R.T.....L.....T.SVI....KSAF.T.A.YL.....F...L..GF-----  
 1 GESQ---FA.I.....T...I.D.I..L....DV..L..K.....V.A.I  
 96 ..L..TL...N...L.L.--T.....M...D.HLA.-.REHQ---FT.I.....T.M..D.IL.L....EV.....K.....V.A.V  
 96 F.IN.T....N.F.GGAS--.....A...L.YG.N.-QKRL---FT.I....P..ITVSS.FEA.HV.L.V.E..V..LTRK.....I.A.V  
 97 ..LQ.T....K.F.GGA.PLG.....L.M...Q.VGIQ-LRRPL---FQ..T.V...Q..TIR..ASGSV.L.V.RC.L.RUTRR.L.....HNP.A.V

194 SLIAVRVYRKCPRVIONGAVFOETLSGAESTSLVAARGTCISNA---EEVDVPIKLYCNGDGEWLVPIGRCMCRPGYESVENGTVCRGCPSGTFKASQG  
 173 ...L.A..K..SNT.AGF.I.P...T...P...I.P...PQ.---V..S..L.....M.V.A.T.AA...PAMKD.Q.QA.GP.....SK..  
 141 -----FK...S.V..F.I.P.MT.....T.....P.....M.....T.KA...PEN.-VA..A.A.....  
 56 A.VS.....K...LTVR.L.Q.PD.IT..DTS....EV..S.VN.S---.K...-M..GA.....N.L.NA...ERNG--E.OA.KI.YY..LST  
 190 A.VS...YFK...FTVK.L.M.PD.VPM-D.Q...EV..S.VNHS---K.EEP.-M..STE.....K.L.NA...ERGF--A.QA.RP.FY...A.  
 190 A.IS...Y.K...ELL.GL.H.P..IA.SDAP..ATVA...VDH.VVPPGEE.-RMH.AV.....Q.L.OA...K..D--A.QA.SP.F..FEAS  
 193 A.VS.....QR..ETLNGL.Q.PD..P.---PAG..EVA...LPH.RASPRPSGAPRMH.SP... ..V...H.E....EGGS.EA.VA....SYRMDMD

FIG. 1A

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[illegible]

Cek5	651	L-PGKREIFVAIKTLKSGYTEKQRDFLSEASIMGQFDHPNVIHLEGVWTKSSPVMIITEFMENGSLDSFLRQNDGQFTVIQLVGMRLRGIAAGMKYLADM
Cek10	626	-..R.....V...R.....I.....R.....CA.....L.....SE..
Cek6	608	-...Y...A..S.....I.R.....R.....A.....E.....
Cek9	268	H-...YT.....DE..E.....E.....R...V.....KE...S.L.....R..S..
Cek8	505	V-...C.....A..D.....I.....CK...Y.....A..K..R.....GS.....S..
Cek7	161	-Q...FP.....V.....G.....I.....K...V..Y.....T.KK.....S.....S..
Cek4	642	-.S.K..S.....A.....G.....I.....K...V..Y.....KH.A.....S.....S..
Eck	634	TSS..K.VP.....A.....V..G.G.....S.H.I.R...IS.YK.M...Y...A..K..EK..E.S.L.....N..
Eph	653	-.SQDCKT.....DTSPGG.WWN..R..T.....S..HIL.....RK.I.....AA..A...ERED.IVPG..A..Q...S..N..SNH

**FIG. 1C**



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Cek5 750 NYVHRDLAARNILVNSNLCKVSDFGLSRFELEDDTSDPTYTSALGKGIPIRWTAPEAIOYRKFTSASDVWSYGIVMWEVMSYGERPYWDMTNQDVINAIE  
 Cek10 725 .....PA.....S.....A.....S.....V.....  
 Cek6 707 .....Y.Q.....S.....V.....A.....F.....S.....  
 Cek9 367 .....A.N.....G.....C.....V.....S.....S.....  
 Cek8 604 S.....M.V.....-PEAA..TR.....A.....S.....S.....  
 Cek7 260 G.....I.....V.....-PEAA..TR.....AF.....E.....K.V.  
 Cek4 741 G.....I.....V.....-PEAA..TR.....S.....A.....L.....E.SF.....K.VD  
 Eck 734 .....V.....-PEA..TS.....S.....F.....T.....ELS.HE.MK..N  
 Eph 752 .....Q.C.....T.L.D.--F.G..ETQ-.....AH.I.T.....F.....L.F.DK..GE.S..E.MKS..



Cek5 850 QDYRLPPMDCPNALHQLMDCWQKDRNHRKFGQIVNTLDKMIRNPNSLKAMAPLSSGVNPLLDRTIPDYTSFNTVDENLDAIKMSQKESFASAGFT  
 Cek10 825 .....T.....VR.....L.....A.....L.....AA.....VI.SVQ....SQ.....V.....T.T..GD.....GR...N.VN...A  
 Cek6 807 .....A.....T.....RLAE.....A.....TV.TITAVPSQ.....S...F.A.TS.ED..S.V.....RDN.L.....  
 Cek9 467 .....P...TV..L.....VQ.....E...SA.....K.SA...TGIG..RPSQ...SNSP..FP.LSNAH.....GR...N.DQ..LI  
 Cek8 702 EG.....I.....E.SD.....M...L.....RTGSE..RPSTA...PSS.EFSAVVS.SD..Q....ER..DN.TA..Y.  
 Cek7 358 EG.....S.....A..Y.....S...DE..SM...L.....S...TLVNA..R.SNL.VEHSPVSGGAYRS.G...E....GR.T.I.MEN.YS  
 Cek4 839 EG.....A..Y.....N.....E...SI...L.....S...IITNAAARPSNL...QSN.I.SA.R.AGD..NGFRTG.C.GI.TGVEYS  
 Eck 832 DGF...T.....S.IY...MQ...QE.AR...AD..SI...L..A.D...TL.DFDPR.SIR.PSTSGSEGVP.R..S...ES...Q..T.H.MA..Y.  
 Eph 849 DG.....V...AP.YE..KN..AY..AR..H.QKLOAH.EQLIA..H..RTI.NFDPR.T.R.PSISGS.GIPYR..S...ES.R.KR.IIH.H...LD

FIG.ID

Cek5 950 TFDIVSQMTVEDILRVGVTLAGHQKKILNSIQWMRAQMNIQSVEV  
 Cek10 924 S..L.A...A..L..I.....S...D..L...TLP.Q.  
 Cek6 907 SLQL.A...S..L..I.....S...V..S.SPTSMA  
 Cek9 567 ...VI.R..L..LQ.I.I..V.....L.KVHL..LEP...  
 Cek8 802 .LEA.VH.NQD.LA.I.I.AIT..N...S.V.A..S..Q.MHGRM.PV  
 Cek7 458 SM.S.A.V.L..-----ESPCE.WSLTLHPLFPTGY.T  
 Cek4 939 SC.TIAKISTD.MKK...V.P....VS..KTLTHTKNSPVV  
 Eck 932 AIEK.V...ND..K.I..R.P....R.AY.IJGLKD.V.TVGIP  
 Eph 949 .MEC.IEL.A..LTOM.I..P....R..C...GFKD

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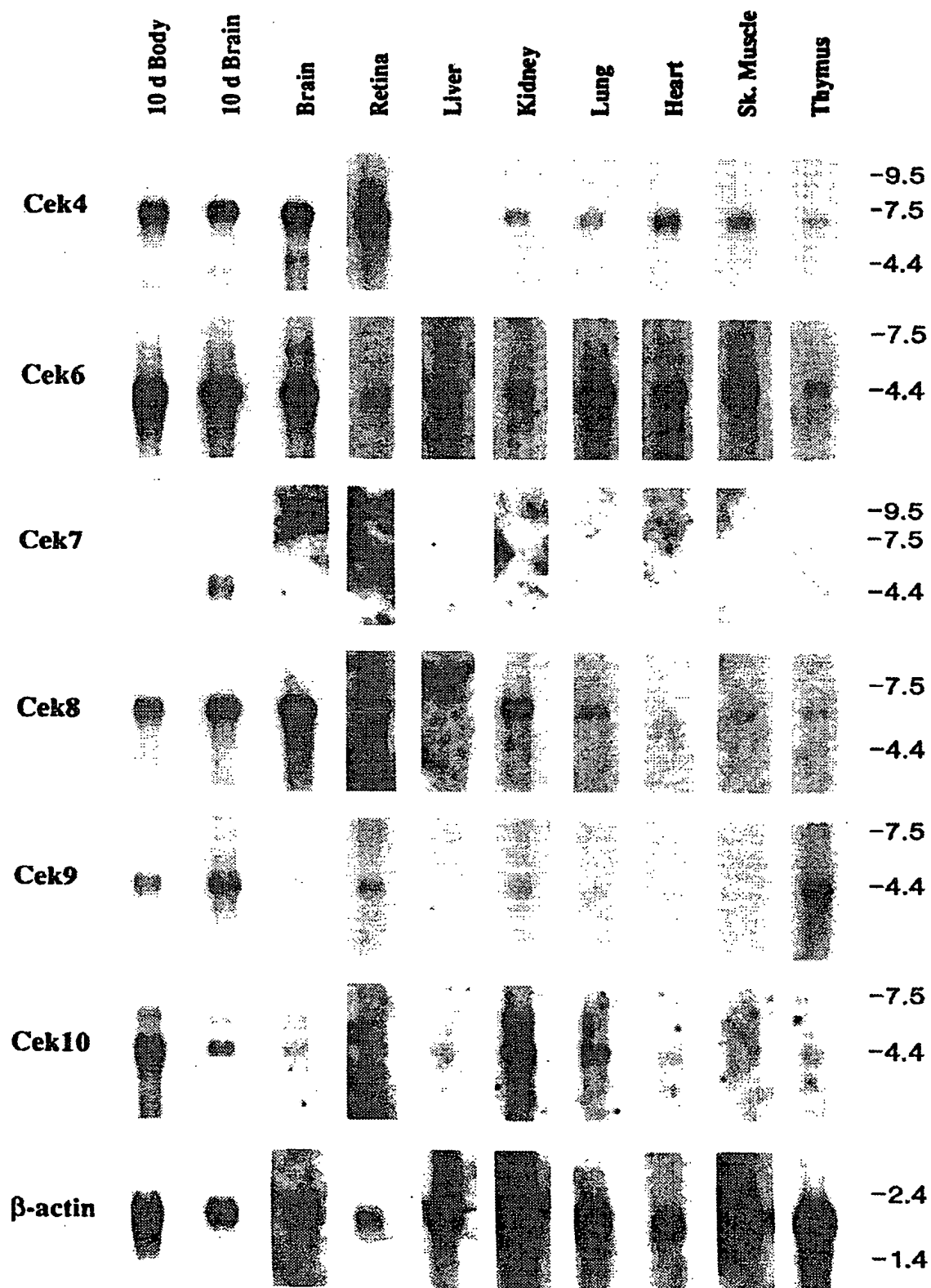


FIG. 2

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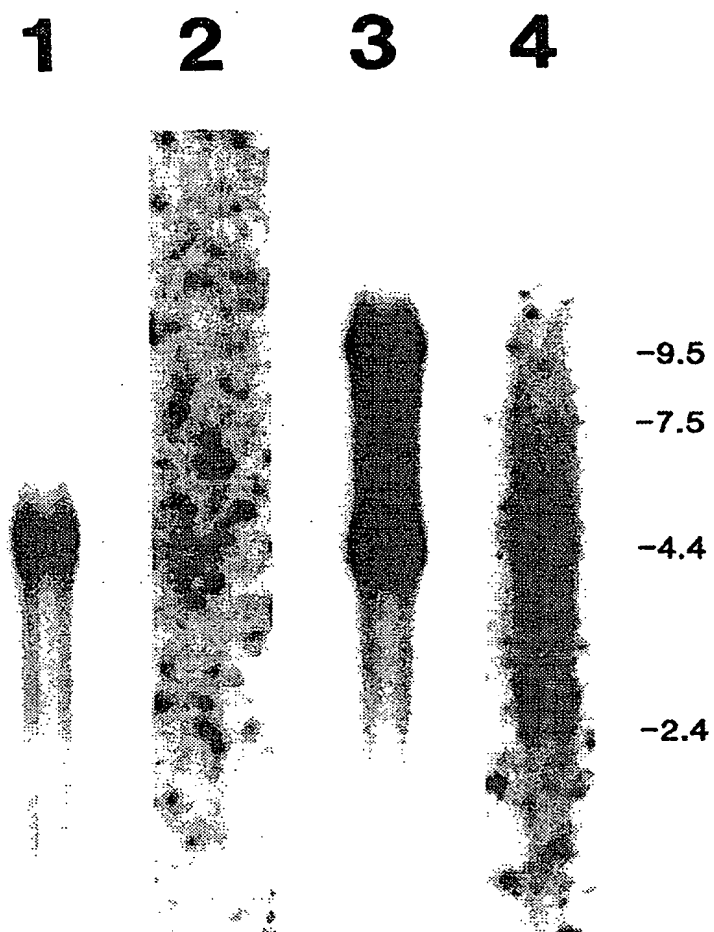


FIG. 3

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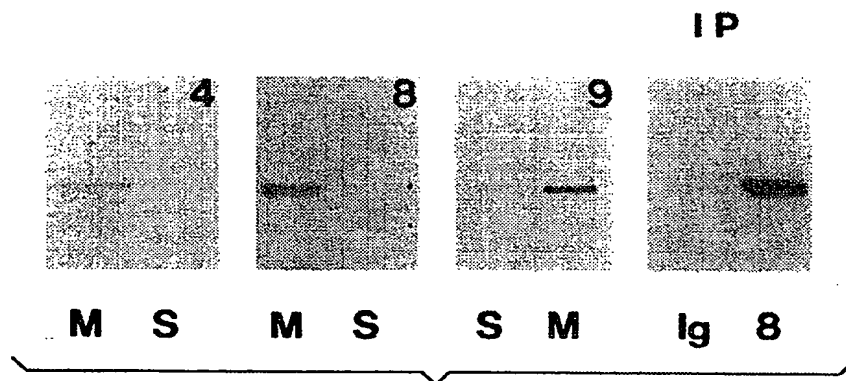


FIG. 4

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FIG. 5A

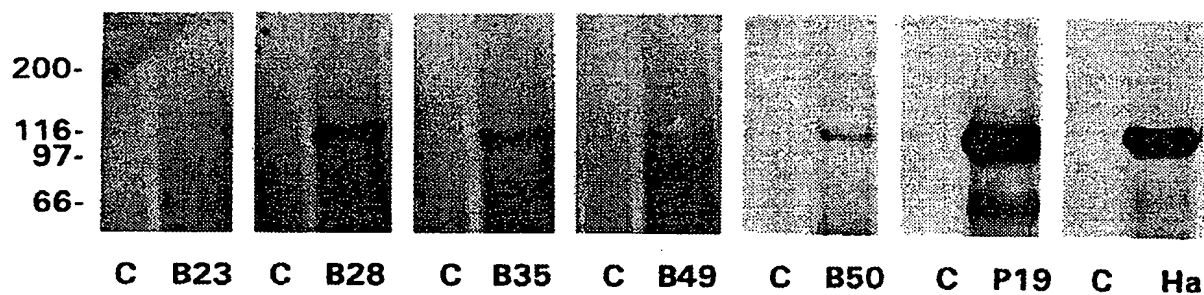


FIG. 5B

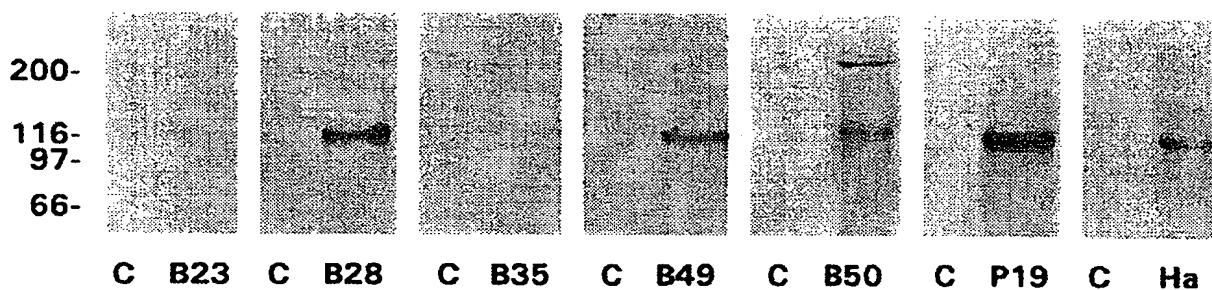


FIG. 5C

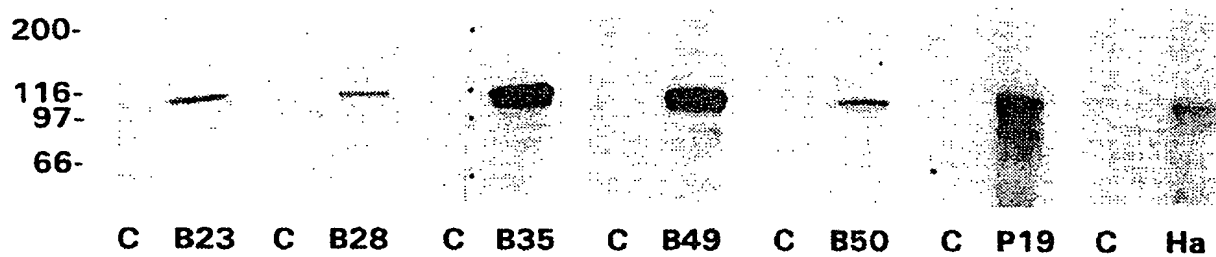


FIG. 5D

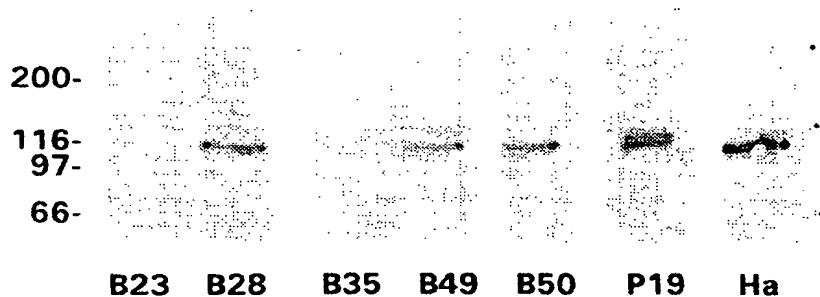


FIG. 6A

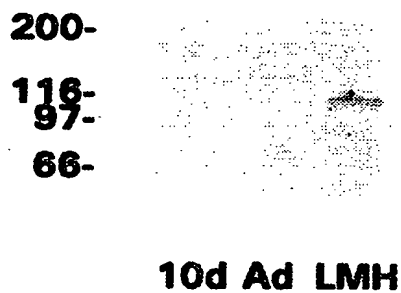


FIG. 6C

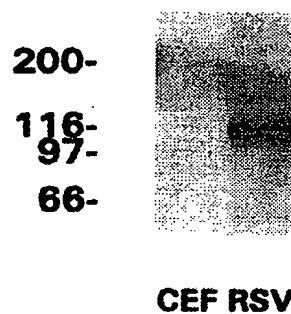


FIG. 6D



FIG. 6B

FIG. 6E

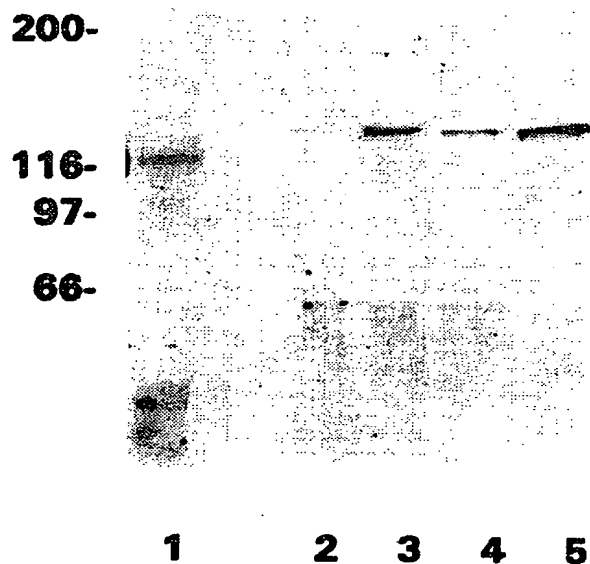
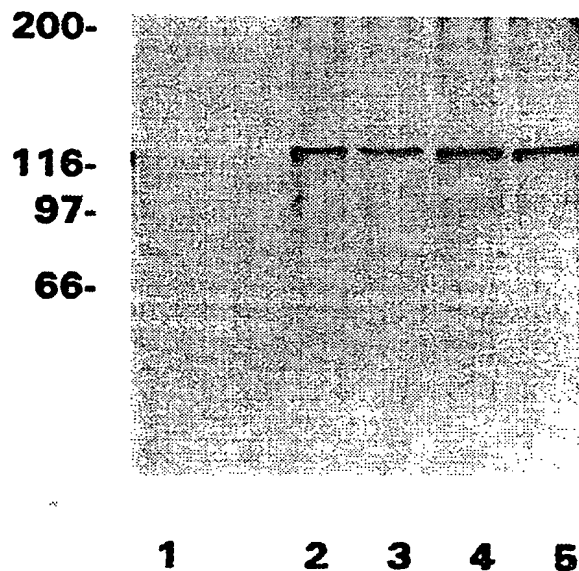


FIG. 6F



**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(6) : C12N 15/00, 9/00

US CL : 435/240.2, 252.3, 320.1, 194; 536/23.2, 23.5

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/240.2, 252.3, 320.1, 194; 536/23.2, 23.5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
noneElectronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
Dialog, APS**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Oncogene, Volume 320, issued 1992, Gilardi-Hebenstreit et al., "An Eph-related receptor protein tyrosine kinase gene segmentally expressed in the developing mouse hindbrain", pages 2499-2507, see entire document.	1-9
Y	Cell Regulation, Volume 2, issued July 1991, E. B. Pasquale, "Identification of chicken embryo kinase 5, a developmentally regulated receptor-type tyrosine kinase of the Eph family", pages 523-534, see entire document.	1-9

☒ Further documents are listed in the continuation of Box C.
 ☐ See patent family annex.

*A*	document defining the general state of the art which is not considered to be of particular relevance	*T*	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*E*	earlier document published on or after the international filing date	*X*	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*L*	document which may throw doubt on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Y*	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*O*	document referring to an oral disclosure, use, exhibition or other means	*Z*	document member of the same patent family
*P*	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

22 NOVEMBER 1994

Date of mailing of the international search report

10 JAN 1995

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## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Proceedings of the National Academy of Sciences USA, Volume 89, issued March 1992, Wicks et al., "Molecular cloning of HEK, the gene encoding a receptor tyrosine kinase expressed by human lymphoid tumor cell lines", pages 1611-1615, see entire document.	1-9

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**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING**

This ISA found multiple inventions as follows:

- I. Claims 1-9 drawn to the DNA, vector, host cell and method of making protein.
- II. Claims 10-13, drawn to the enzyme.
- III. Claims 14-17, drawn to a method of using the enzyme of Group II.

The inventions listed as Groups I-III do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The DNA Group I and the protein of Group II are not chemically related, and they are independent and distinct inventive concepts. The DNA possesses utility other than encoding the protein, such as in a hybridization assay or as a probe. The DNA of Group I is not related to the method of Group III for similar reasons, as the method of Group III does not involve the DNA.

Groups II and III are related as a second product and method of use. The method may be used with a materially different enzyme, such as one from another source.